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VITAMIN C AND WOUND HEALING*

I. Experimental Wounds in Guinea Pigs

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BOSTON

THAT the tensile strength of healing wounds is lowered in the presence of scurvy in guinea pigs was established by Lanman and Ingalls[1] in 1937 and confirmed by Taffel and Harvey.[2]

The work of Bessey[3] has provided a satisfactory method of determining the ascorbic acid content of tissues, and the experiments reported in this study were undertaken to determine the concentration of vitamin C in healing wounds in guinea pigs under a variety of dietary conditions, and to correlate the ascorbic acid content with the tensile strength of these wounds.

METHODS

After suitable dietary preparation, under ether anesthesia, a midline abdominal incision was made in each guinea pig, extending from the xiphoid to a point just below the umbilicus. A strip of tissue adjacent to the wound, consisting of the full thickness of the abdominal wall and weighing about 2 gm., was excised for ascorbic acid assay. This specimen is called "control tissue" in the various tables that appear below. The peritoneum and muscular layers were then closed in a single layer with a running suture of fine silk, and the skin was closed in a similar manner.

At the end of a suitable period of wound healing, the skin sutures were removed, and the healing wound excised, including the full thickness of the abdominal wall in a strip about 0.6 cm. in width, with the line of incision running down its center. This tissue was assayed for ascorbic acid and appears under the heading "abdominal scar" in the tables. Portions of abdominal wall adjacent to the excised scar and similar portions at a distance from it were removed for comparative assay. These appear as "adjacent abdominal wall" and "distant abdominal wall" in the tables. Vitamin C determinations were also done on the livers and kidneys of these animals.

The term "house diet" is used to describe the usual one of grain, hay, green vegetables and water. As a scorbutic diet, we have found the one described by McCullough[4] most satisfactory. Animals can be successfully maintained on this diet for considerable periods. Its percentage composition is as follows:

Whole-milk powder (inactivated at 120°C. for two hours)	40.5
Ground, rolled oats	25.0
Bran	25.0
Dried brewer's yeast	5.0
Cod-liver oil	3.0
Sodium chloride	1.0
Ferric citrate	0.5

To afford a high intake of vitamin C, either the house diet or the scorbutic diet was supplemented by 33 mg. of ascorbic acid in 5 cc. of water twice daily. This solution was fed to the animals by medicine dropper and was usually taken without difficulty. The dosage is considerably larger than that reported by Zilva[5] and by Ecker and Pillemer[6] as necessary to maintain tissue saturation in the guinea pig, and should certainly provide an excess of ascorbic acid even in the presence of a possible increased demand due to the healing wound.

RESULTS

Control Animals

The ascorbic acid content of various animal tissues has been studied by several workers.[7-15] However, because of differences in methods of assay and varying experimental conditions, the results of these investigations are not strictly comparable to the studies reported here, and will not be referred to in detail.

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To obtain control figures, the ascorbic acid content of the abdominal wall was determined on 19 guinea pigs on a scorbutic diet for two weeks or more. The average concentration was 0.23 mg. per 100 gm. Similar determinations were made on 17 animals on a high vitamin C diet for two weeks or more, and it was found that the average level was 1.51 mg. per 100 gm.

We believe two weeks to be an adequate period to establish a tissue level of ascorbic acid on a given diet. The results of assays of the abdominal wall, liver and kidney, made at intervals of one, two and three weeks, on animals on a high or low vitamin C intake appear in Table 1. There

TABLE 1. *Tissue Assays of Ascorbic Acid on Control Animals on Diets Varying in Vitamin C Content.*

WEEKS	ABDOMINAL WALL mg./100 gm.	LIVER mg./100 gm.	KIDNEY mg./100 gm.
HOUSE DIET			
3+	0.47	2.82	1.11
3+	0.65	1.82	1.35
HIGH VITAMIN C DIET			
1	1.99	19.35	5.57
2	2.28	11.26	5.94
3	2.52	14.41	6.49
SCORBUTIC DIET			
1	0.31	1.42	1.49
2	0.08	0.43	2.99
3	0.59	1.13	0.21

seems to be no essential difference between the levels attained at the end of one week and those at longer intervals. We have therefore taken a period of two weeks as being adequate to establish tissue levels of ascorbic acid corresponding to the intake of vitamin C.

It is interesting that the house diet, which has apparently been entirely satisfactory over a period of years, and on which guinea pigs thrive for indefinite periods, produces tissue levels only slightly higher than the scorbutic diet. This wide variation in the amount of ascorbic acid necessary for protection against scurvy and that required to produce tissue saturation has been stressed by Zilva[5] and by Ecker and Pillemer.[6]

Experimental Animals

Preoperative and postoperative scorbutic diet. Ten guinea pigs were maintained on a scorbutic diet for two weeks. At the end of this time, an abdominal incision was made, and a control biopsy obtained. The scorbutic diet was continued postoperatively.

At the end of arbitrary intervals, varying from four to fourteen days, the animals were killed and tissue assays done, as previously described. The results of these determinations are shown in Table 2.

The average postoperative interval was nearly ten days, and there was no significant variation in the tissue levels at the shorter and longer postoperative intervals. All the tissue levels were low, and the averages show that there was no increase in the concentration of ascorbic acid in the heal-

TABLE 2. *Assays of Ascorbic Acid in Tissues of Animals on a Preoperative and Postoperative Scorbutic Diet.*

CONTROL TISSUE	POSTOPERATIVE DAY ON WHICH ANIMAL WAS KILLED	AUTOPSY TISSUES				
		ABDOMINAL SCAR	ADJACENT ABDOMINAL WALL	DISTANT ABDOMINAL WALL	LIVER	KIDNEY
ABDOMINAL WALL						
mg./100 gm.		*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*
0.14	4	0.19	0.33	—	1.15	0.16
0.28	4	1.13	0.14	0.08	1.30	0.98
0.15	5	0.04	0.21	—	1.19	0.34
0.09	9	0.24	0.11	—	0.73	0.16
0.21	9	0.18	0.05	—	0.58	0.32
0.28	9	0.27	0.20	0.25	0.63	0.75
0.09	14	0.10	0.17	—	0.44	0.59
0.10	14	0.33	0.01	—	0.81	—
0.09	14	0.12	0.06	0.23	0.59	0.19
0.15	14	0.28	0.16	0.22	1.13	0.39
Average						
0.25	9.6	0.29	0.14	0.20	0.86	0.43

ing wound. Assays of the abdominal wall, both adjacent to and at a distance from the healing area, showed some decrease below the level found in the control biopsy taken at operation.

Preoperative and postoperative high vitamin C diet. After a preliminary period of two weeks on a high ascorbic acid intake, 10 animals were subjected to the same operative procedure as that in the preceding group. At postoperative intervals of four to fourteen days, with an average of nine days, the animals were killed and the tissue assays of ascorbic acid were done. The results appear in Table 3.

TABLE 3. *Assays of Ascorbic Acid in Tissues of Animals on a Preoperative and Postoperative Diet High in Vitamin C.*

CONTROL TISSUE	POSTOPERATIVE DAY ON WHICH ANIMAL WAS KILLED	AUTOPSY TISSUES				
		ABDOMINAL SCAR	ADJACENT ABDOMINAL WALL	DISTANT ABDOMINAL WALL	LIVER	KIDNEY
ABDOMINAL WALL						
mg./100 gm.		*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*
1.08	4	7.39	4.93	—	11.73	6.92
2.24	4	6.74	3.67	—	15.21	4.85
1.28	4	4.63	3.18	2.72	4.88	3.74
1.36	9	6.83	2.96	2.97	18.16	4.53
1.51	9	9.71	4.70	5.31	22.02	6.05
1.90	9	6.15	1.85	1.69	5.53	4.14
1.23	9	5.62	3.15	3.09	4.68	2.88
2.09	14	6.70	3.39	2.71	7.63	3.98
0.69	14	7.15	1.21	1.07	4.22	1.99
2.29	14	4.38	2.29	2.04	1.77	1.01
Average						
1.57	9.0	6.53	3.13	2.70	9.58	4.01

Again, there was no significant difference in the results obtained at the shorter and longer post-

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operative intervals. However, there was a marked increase in ascorbic acid content in the healing wound over the concentration in the control biopsy of the abdominal wall. The tissue of the abdominal wall adjacent to the healing wound, taken at autopsy, showed a considerable increase in vitamin C content, and a slight increase was shown in the abdominal wall at a distance from the wound. The assays of liver and kidney showed levels uniformly much higher than those obtained on similar animals on a scorbutic diet, but not quite so high as those in the 3 animals on a high ascorbic acid diet on which no operation was done (Table 1). The small number of animals in the last group makes it impossible to say whether or not this difference was significant. It seems unlikely, considering the very large doses of ascorbic acid administered to both groups.

TABLE 4. *Assays of Ascorbic Acid in Tissues of Animals on a Preoperative Scorbutic Diet and a Postoperative High Vitamin C Diet.*

Control Tissue Abdominal Wall	Postoperative Day on Which Animal Was Killed	Autopsy Tissues: Abdominal Scar	Adjacent Abdominal Wall	Distant Abdominal Wall	Liver	Kidney
mg./100 gm.		*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*
0.21	4	4.53	2.42	2.77	7.91	4.23
0.16	9	3.90	1.37	1.22	4.47	2.28
0.07	9	5.13	2.73	2.87	0.54	2.18
0.16	9	4.32	1.99	1.63	5.03	2.59
0.09	14	4.04	2.50	0.98	2.89	1.65
0.27	14	3.81	1.83	2.49	2.74	2.53
Average						
0.16	9.9	4.29	2.14	1.99	3.93	2.58

TABLE 5. *Assays of Ascorbic Acid in Tissues of Animals on a Preoperative High Vitamin C Diet and a Postoperative Scorbutic Diet.*

Control Tissue Abdominal Wall	Postoperative Day on Which Animal Was Killed	Autopsy Tissues: Abdominal Scar	Adjacent Abdominal Wall	Distant Abdominal Wall	Liver	Kidney
mg./100 gm.		*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*	*mg./100 gm.*
0.0	4	0.42	0.17	0.33	0.18	0.77
0.77	9	0.82	0.38	0.40	1.78	0.73
1.05	9	0.11	0.18	0.14	0.66	0.75
1.35	14	0.59	0.22	0.27	0.54	0.44
Average						
0.79	9.0	0.49	0.24	0.29	0.79	0.67

Preoperative scorbutic diet and postoperative high vitamin C diet. It seemed desirable to study the relative importance of the preoperative diet and the ascorbic acid intake in the postoperative interval, in determining the ascorbic acid content of the healing wound and other tissues at autopsy. Contrasting experiments were planned, one group of animals receiving a scorbutic diet preoperatively and a high ascorbic acid intake postoperatively. The other group had a diet high in vitamin C preoperatively and a scorbutic diet postoperatively.

TABLE 6. *Tensile Strength of Healing Wounds in Relation to Vitamin C Content.*

	Pressure of Skin Separation	Pressure of Wound Rupture	Vitamin C Content of Scar
	mm. Hg.	*mm. Hg.*	*mg./100 gm.*
Scorbutic Diet			
	?	120	0.21
	80	140	0.47
	60	120	0.24
Average	70	127	0.31
High Vitamin C Diet			
	140	300*	6.89
	160	245	7.74
	120	230	8.28
Average	140	258	7.64

*Wound failed to rupture at 300 mm. Hg.

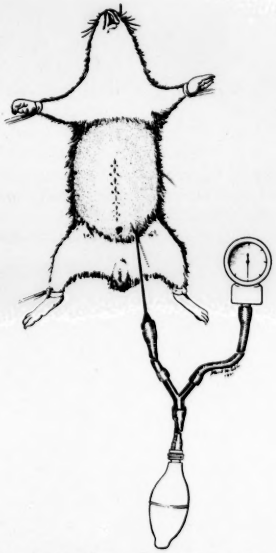

FIGURE 1. *Method of Determining Tensile Strength of a Healing Wound in the Abdominal Wall of a Guinea Pig.*

The peritoneal cavity is inflated until the wound ruptures; the pressure is recorded in millimeters of mercury.

After two weeks on a scorbutic diet, 6 animals were subjected to operation. The operative procedure was the same as that performed in the

preceding groups of animals. Immediately after operation, a high ascorbic acid intake was instituted, and at varying intervals the animals were killed and tissue assays for ascorbic acid done. The results appear in Table 4.

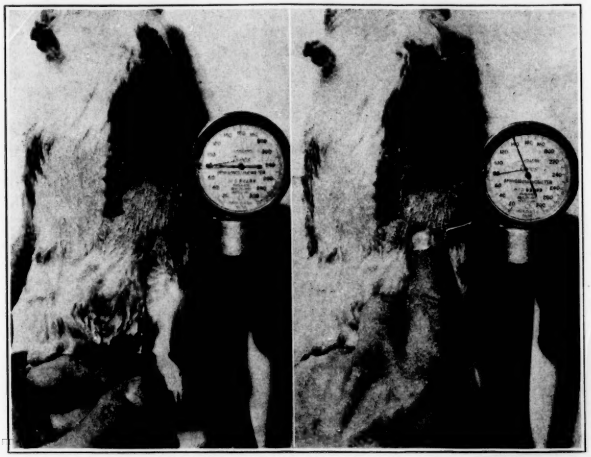

FIGURE 2.
The photograph on the left shows the pressure required to separate the skin; that on the right, to rupture the wound.

The variation of the postoperative intervals from four to fourteen days seemed to make no significant difference in the tissue levels at autopsy. As would be expected, the control biopsy showed a low concentration of ascorbic acid — the same amount as that found for other animals on the same dietary regime (Table 2).

All the changes in tissue levels found at autopsy were similar to those found in animals maintained on a high ascorbic acid intake both preoperatively and postoperatively. The extent of the rise was

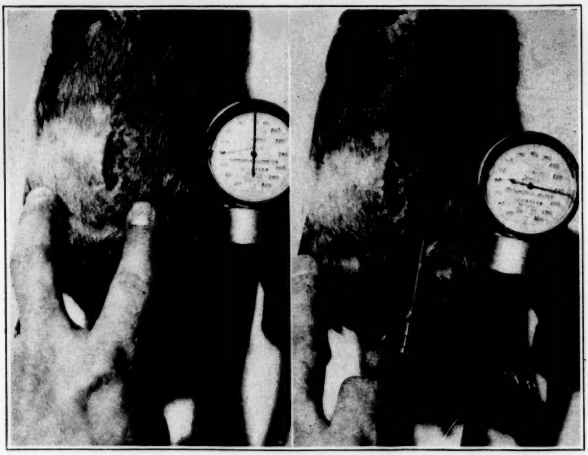

FIGURE 3.
The photograph on the left shows the pressure required to separate the skin; that on the right, to rupture the wound.

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somewhat less in each tissue in the group under discussion.

Preoperative high vitamin C diet and postoperative scorbutic diet. In contrast with the above group, 4 animals were maintained on a high ascorbic acid intake for two weeks before operation, and on a scorbutic diet during the postoperative interval. The results of the ascorbic acid assays on the various tissues appear in Table 5.

Although these animals were saturated with large amounts of ascorbic acid before operation, the tissue levels obtained at autopsy were strikingly similar to those of the group of animals on a scorbutic diet both before and after operation. Why one animal failed to show any ascorbic acid in the control biopsy of the abdominal wall, in spite of the high intake of ascorbic acid preoperatively, is not clear.

Tensile strength and ascorbic acid content of healing wounds. The work of Lanman and Ingalls,[1] establishing the decrease in tensile strength of healing wounds in the presence of scurvy, has already been mentioned. We have attempted to repeat this experiment, correlating the tensile strength of the healing wound with the ascorbic acid content of the healing scar.

Three animals were established on a scorbutic diet. Abdominal incisions were made and sutured in the manner already described. The same diet was maintained postoperatively. Another group of 3 animals was given a diet high in ascorbic acid throughout the experiment, and the same operative procedure was carried out.

Since our previous studies had indicated that the ascorbic acid content of the healing wound was certainly stabilized ten days after operation, the animals were killed at this time, and the tensile strength of the healing scar in the abdominal wall was determined by a method similar to that used by Lanman and Ingalls. An ordinary, long 18-gauge needle was introduced into the peritoneal cavity, and connected by rubber tubing to a rubber bulb and sphygmomanometer (Fig. 1). Air was introduced into the peritoneal cavity until a pressure was attained sufficient to cause rupture of the wound. The pressure, recorded in millimeters of mercury, was noted.

Characteristically, the wounds ruptured in two stages. Skin separation occurred at first, followed at a higher pressure by the rupture of the muscular layer.

The ruptured wounds were then excised and assayed for ascorbic acid content. The results of this experiment appear in Table 6. The average tensile strength in the animals on a high ascorbic acid intake was exactly twice that of the animals on a scorbutic diet, and the vitamin C content of the healing wounds showed the same striking contrast already noted (Tables 2 and 3).

Figure 2 shows a typical wound in a scorbutic animal at the moment of rupture. In Figure 3, the rupture of a wound in an animal on a diet rich in vitamin C is shown.

Summary and Conclusions

Wide variations of the ascorbic acid content of guinea-pig tissues, as measured by Bessey's method of tissue assay, can be caused by a high or low intake of ascorbic acid.

Similar variations of ascorbic acid content can be demonstrated in a healing wound of the abdominal wall, depending on the vitamin C intake.

Animals on a scorbutic diet show essentially no increase in ascorbic acid in the healing area and slightly lowered values in the remainder of the abdominal wall, compared with the level in control biopsies obtained at the time of operation. The liver and kidney also show low levels.

On a high ascorbic acid intake, a striking increase in vitamin C content of the healing wound over that of the control biopsy can be demonstrated. The abdominal wall adjacent to the scar also shows a considerable rise, and a slight increase is found even at a distance from the wound. High levels are also found in the liver and kidney.

In these experimental animals, the tissue level attained by the preoperative administration of ascorbic acid is of much less importance in establishing the optimum ascorbic acid content of the healing wound and other tissues studied than the vitamin C intake during the postoperative period.

The tensile strength of wounds showing a high ascorbic acid content is much greater than that of those with low vitamin C values.

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VITAMIN C AND WOUND HEALING*

II. Ascorbic Acid Content and Tensile Strength of Healing Wounds in Human Beings

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BOSTON

IN recent years, a considerable amount of evidence has established the efficacy of vitamin C in wound healing in animals. Lanman and Ingalls[1] first made direct measurements of the tensile strength of healing wounds in guinea pigs and found it decreased in the presence of scurvy. In the preceding paper,[2] we reported the results of studies on the tissue ascorbic acid content of similar wounds in guinea pigs and correlated this with the tensile strength of these wounds. A much higher concentration of vitamin C occurs in the wounds of animals on a high ascorbic acid intake than in those of animals on a scorbutic diet, and the tensile strength of wounds showing a high ascorbic acid content was found to be much greater than that in those with low vitamin C values.

Elaborating on the work of Lanman and Ingalls, Taffel and Harvey[3] studied the effect of partial as well as absolute vitamin C deficiency on the tensile strength of healing wounds in guinea pigs. There was a slightly greater tensile strength at four days after operation in animals with absolute scurvy than in the normal controls. At six days, the tensile strength was markedly inferior to that in normal animals. None of the scorbutic animals survived for a longer postoperative period. In their experiments, a state of partial scurvy was established as follows: after a week on the scorbutic diet supplemented by 5 mg. of ascorbic acid daily, all vitamin C was withheld for two weeks, and then 0.2 mg. of ascorbic acid was given on alter-

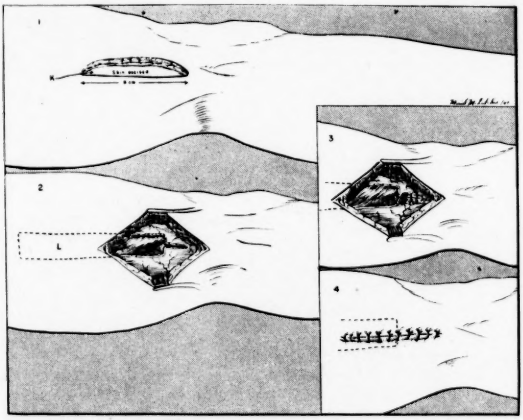

FIGURE 1. *Method of Obtaining Tissue for Ascorbic Acid Assay and Tensile-Strength Determinations.*

1—incision through skin and subcutaneous tissue with excision of a strip of skin for ascorbic acid assay (K); 2—fascia stripped out in the usual manner for repair of the hernia, and for ascorbic acid assay (L), with an incision made in the fascia lata for 2 cm. distal to the area stripped out; 3—incision in fascia closed with fine silk stitches; 4—skin closed in the usual manner.

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nate days. Abdominal incisions were made after ten days on this low vitamin C intake. It is extremely interesting that, although all the animals showed unmistakable gross evidence of scurvy at autopsy, tests for tensile strength on the healing wounds showed a significant decrease below that of normal controls only on the eighth and tenth days after operation. Tests on the fourth and sixth days showed no appreciable variation from the controls, and those on the twelfth and fourteenth days again approached normal.

The effect of prolonged reduced intake of vitamin C on wound healing in an otherwise normal adult human subject has been studied by Crandon, Lund and Dill[4] and by Hunt.[5] In both studies, the histologic appearance of the wound was used as an index of abnormal healing. Crandon, Lund and Dill found that adequate wound healing occurred after the plasma ascorbic acid had been zero for forty-four days and when the white-cell and platelet ascorbic acid level was 4 mg. per 100 cc. A second wound, made when the plasma ascorbic acid had been zero for one hundred and forty-one days and the white-cell and platelet ascorbic acid content had been at zero for sixty-one days, failed to heal in a normal manner after ten days, and showed lack of intercellular substance and capillary formation on histologic examination. The intravenous administration of 1000 mg. of ascorbic acid daily for ten days brought about microscopic evidence of good healing. Hunt[5] reported histologic evidence of healing of an experimental wound in a subject who had been on a reduced vitamin C intake for three months and who had a blood ascorbic acid content of 0.34 mg. per 100 cc. A second experimental wound in the same patient, followed by the administration of large doses of ascorbic acid, showed no macroscopic or microscopic difference from the first wound.

The present studies were undertaken in an attempt to obtain further information regarding the value of vitamin C in wound healing in human beings, by means of direct observations on the tensile strength of healing wounds and a correlation of these with the tissue content of ascorbic acid and plasma ascorbic acid levels.

Methods

Male patients admitted to the hospital for the repair of inguinal hernias who were good surgical risks and on whom the use of fascia lata in the repair was contemplated were selected for these studies.

During the preliminary period of two to four days, the plasma ascorbic acid was determined by the method of Mindlin and Butler,[6] and the daily urinary output measured by Bessey's[7] method. Throughout the hospital stay, these patients were maintained on a diet containing 100 mg. of vitamin C daily. Supplementary ascorbic acid was given to some patients before and after operation, as described in the case reports.

Studies were carried out on a total of 6 patients. Of these, 5 had unilateral hernias, and 1 had bilateral hernias.

The operations were performed under spinal anesthesia, and the usual hernia repair was done. Fascia lata was obtained through a longitudinal skin incision about 8 cm. in length just above the knee on the lateral aspect of the thigh. A strip of skin, weighing about 2 gm., was excised

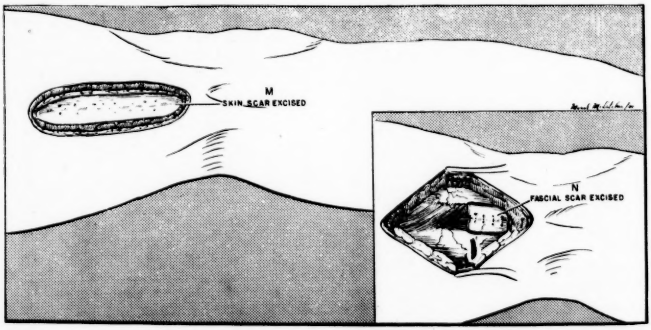

Figure 2. *Method of Subsequently Obtaining Tissue for Ascorbic Acid Assay and Tensile-Strength Determinations.*

The skin scar is excised (M), exposing the healing fascial scar (N), which is also excised. The skin is then closed in the usual manner.

from the edge of this wound for ascorbic acid assay as a control biopsy. The fascia was removed by means of a stripper, and in addition to that necessary for the hernia repair, enough was removed for ascorbic acid assay. The tissue ascorbic acid content was determined on the excised skin and fascia by the method described by Bessey[7] and previously employed in our animal experiments. Distal to the area of excised fascia, a longitudinal incision 2 cm. in length was made in the fascia lata, parallel to its fibers, and this was closed with interrupted sutures of fine silk. The skin was then closed in the usual manner with interrupted silk (Fig. 1).

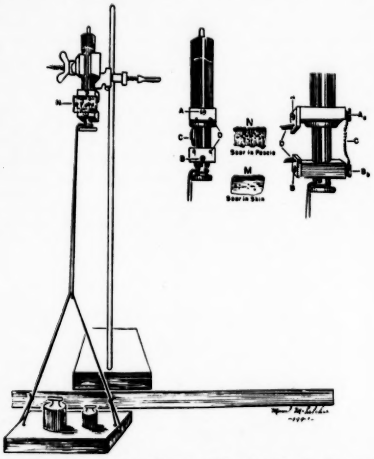

FIGURE 3. *Method for Determining the Tensile Strength of Healing Scars in Skin and Fascia.*

The apparatus consists of a 5-cc. glass syringe, with collars mounted on the barrel and plunger (Aa and Bb). On each collar a bar is attached, pivoted at its center (A and B). Two pins (D), spaced 1 cm. apart, are mounted on each bar, and the tissue to be tested (M or N) is placed on these four pins. Tension is applied by weights on the platform. The pull necessary to rupture the scar is recorded in grams.

The wound was allowed to heal for ten days, the skin sutures being removed on the eighth day. At the end of ten days, under novocain block anesthesia, the skin incision in the thigh was excised with a margin of slightly less than 1 cm. of skin on each side of the scar; the incision in the fascia was excised with the same margin of tissue (Fig. 2).

The tensile strength of the healing wound and the tissue ascorbic acid content were determined on the skin and fascia. In some cases, enough skin was available to allow duplicate determinations. The tensile strength was measured by the application of a direct pull on the healing scar, as illustrated in Figure 3. The apparatus consisted of a 5-cc. glass syringe, with collars mounted on the barrel and plunger. Each collar carried a bar, pivoted at the center, bearing two pins spaced 1 cm. apart. The pivot provided an equalized pull on the tissue mounted on the pins, when tension was applied by means of weights placed on the platform.

As a result of duplicate determinations on portions of the same skin scars, it became evident that there was considerable variation by this method, and we believe that only gross differences should be considered significant.

CASE REPORTS

CASE 1. A. A., a 65-year-old man, was admitted for repair of a right inguinal hernia. The plasma ascorbic acid was 0.60 and 0.66 mg. per 100 cc. on two occasions before operation, and no significant variation from this level occurred following operation.

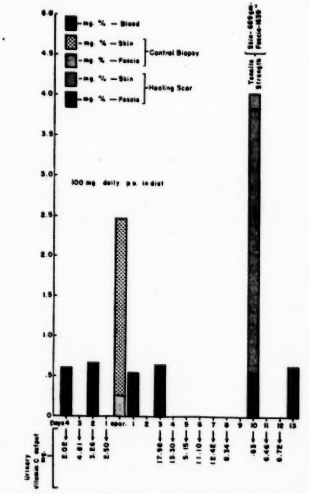

FIGURE 4. *Case 1.*

Determinations of ascorbic acid in the blood plasma, in control biopsies of skin and fascia and in healing skin and fascial scars are shown. Urinary excretion of vitamin C is recorded in twenty-four-hour amounts, and the tensile strengths of the skin and fascial scars are listed. Where columns are superimposed, the actual amount of each component is the maximum height of the column above the abscissa.

Control biopsies of skin and fascia from the left leg were obtained at the time of herniorrhaphy. The skin

showed an ascorbic acid content of 2.49 mg., and the fascia one of 0.29 mg. per 100 gm. At the end of 10 days, the skin and fascia scars were excised. The skin showed a tensile strength of 700 gm. and a vitamin C content of 4.04 mg. per 100 gm. The fascia scar broke at a tension of 1600 gm. and contained 3.88 mg. of ascorbic acid per 100 gm. The complete data on this patient appear in Figure 4.

Case 2. E. J. L., a 36-year-old man, was admitted for repair of a left inguinal hernia. The preoperative plasma ascorbic acid was 0.20 mg. per 100 cc. on two occasions. Control biopsies of skin and fascia lata showed a vitamin C

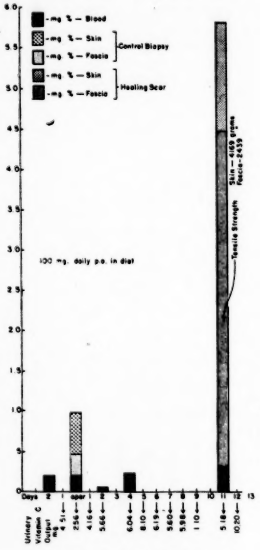

Figure 5. *Case 2.*

content of 0.99 mg. and 0.48 mg. per 100 gm., respectively. After healing for 10 days, the skin scar had a tensile strength of 4200 gm. and an ascorbic acid content of 5.82 mg. per 100 gm. The fascia scar ruptured at 1400 gm. with a vitamin C content of 4.48 mg. per 100 gm.

In this patient, except for a transient drop after operation, the plasma ascorbic acid showed no significant variation during the postoperative interval. This transient fall has been previously noted by various workers. The studies on this patient are shown in Figure 5.

Case 3. J. S., a 24-year-old man, entered the hospital because of a left inguinal hernia. Two preoperative plasma ascorbic acid determinations showed 0.31 and 0.26 mg. per 100 cc. Control biopsies of the skin and fascia lata were taken. The skin contained 0.84 mg. and the fascia 0.11 mg. of ascorbic acid per 100 gm. From the day of operation, 1000 mg. of vitamin C was given daily, in addition to the 100 mg. contained in the regular diet. The plasma ascorbic acid level rose promptly and remained between 0.68 and 1.01 mg. per 100 cc. during the postoperative interval. A corresponding rise in urinary output of vitamin C occurred.

After healing for 10 days, the skin and fascia scars were excised from the leg. The skin scar had a tensile strength of 1500 gm. and an ascorbic acid content of 5.23 mg. per 100 gm. The healing fascia broke under a tension of 1200 gm., with a vitamin C tissue level of 7.65 mg. per 100 gm. The complete data on this patient appear in Figure 6.

Case 4. F. W., a 62-year-old man, proved to be the most interesting patient studied. He had bilateral inguinal hernias, which were repaired separately. He also had the lowest preoperative plasma ascorbic acid level in the group — 0.09 and 0.08 mg. per 100 cc. on two determinations. There was no clinical evidence of scurvy.

At the first operation, the right hernia was repaired, and control biopsies of skin and fascia were obtained from the left leg. These tissues both showed a tissue ascorbic acid level of zero. No ascorbic acid, other than the 100 mg. daily in the diet, was given after operation, and the plasma ascorbic acid remained at the same low level.

At the end of 10 days, the left hernia was repaired, fascia from the right leg being used, and control specimens of skin and fascia were obtained from the new incision. They also showed a zero level of ascorbic acid. At the same

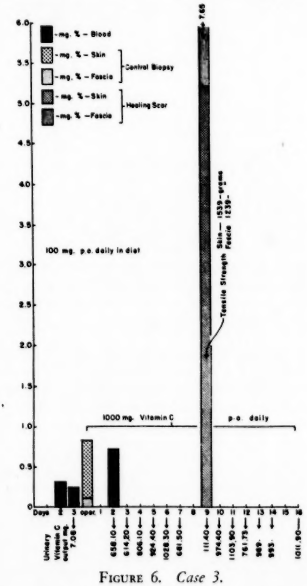

Figure 6. *Case 3.*

time, the 10-day-old scars in the skin and fascia of the left leg were excised. The skin scar had a vitamin C level of 0.67 mg. per 100 gm. and a tensile strength of 400 gm. (average of two determinations). The healing fascia had a tissue level of ascorbic acid of zero and ruptured at a tension of 300 gm.

The patient was then given 1000 mg. of ascorbic acid by mouth daily, in addition to that in the regular diet, and the blood ascorbic acid promptly rose to above 1.0 mg. per 100 cc. and remained at this level, with a corresponding increase in the urinary output of ascorbic acid.

Ten days after the second operation, the healing skin and fascia scars were excised from the right leg. An ascorbic acid assay on the skin gave a result of 6.77 mg.

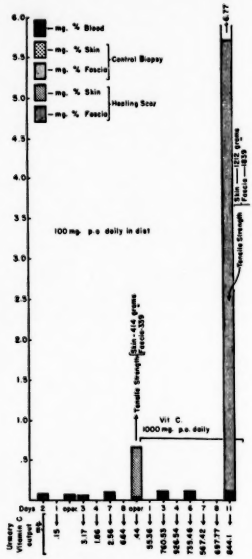

FIGURE 7. *Case 4.*

Tissue assay of vitamin C on the control biopsies of the skin and fascia at both operations and of the healing fascia excised at the second operation were all zero, and so do not appear.

per 100 gm., and the scar separated with a pull of 1200 gm. (average of three determinations). The fascia contained 5.73 mg. of vitamin C per 100 gm., and the scar had a tensile strength of 1800 gm. Figure 7 shows the results of these studies in graphic form.

CASE 5. A. D., a 26-year-old man, was recommended for admission to the hospital because of a left inguinal hernia. The plasma ascorbic acid was found to be 0.26 mg. per 100 cc., and he was given 200 mg. of vitamin C daily for 2 weeks prior to admission. After a week, the plasma ascorbic acid was 0.98 mg. per 100 cc., and on admission it was 0.81 mg. The patient was given the same dose (200 mg.) of ascorbic acid daily in addition to 100 mg. in the diet, and on the day of operation the plasma ascorbic acid was 0.87 mg. per 100 cc. The hernia was repaired, and skin and fascia were obtained from the right leg for vitamin C assay. The skin contained 0.78 mg. and the fascia 0.17 mg. of ascorbic acid per 100 gm.

Except for the day of operation, when no ascorbic acid was given, the daily intake was maintained at a total of 300 mg. of vitamin C daily. Ten days after operation, the healing skin and fascia scars were excised from the leg. In addition, a small pigmented nevus was removed from the back, together with a margin of surrounding normal skin.

The healing skin showed 5.54 mg. of ascorbic acid per 100 gm., and the scar ruptured with a pull of 600 gm. (average of three determinations). The fascia had a vitamin C level of 7.24 mg. per 100 gm. and a tensile strength of 1100 gm. The pigmented nevus was discarded, and the surrounding skin was assayed for vitamin C. A level of 1.88 mg. per 100 gm. was obtained. These studies appear in Figure 8.

CASE 6. T. D., a 48-year-old man, was admitted to the hospital because of a large left inguinal hernia. A plasma ascorbic acid determination 2 weeks before admission showed a level of 0.73 mg. per 100 cc. The patient was given 600 mg. of vitamin C daily, and this was continued, together with the 100 mg. in the regular diet, until 10 days after operation, except for the day of operation, when he received none. The plasma ascorbic acid was 1.26 mg. per 100 cc. on admission, and except for a transient

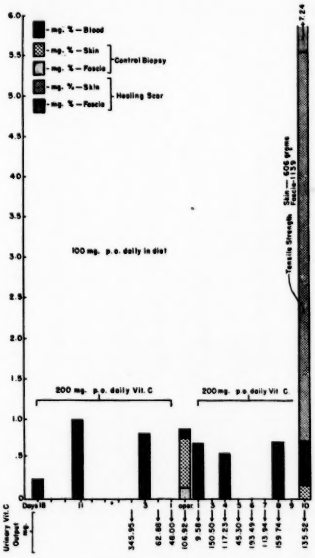

FIGURE 8. *Case 5.*

drop after operation, it remained above 1.0 mg. per 100 cc. until the supplementary dose of vitamin C was withdrawn.

At operation, the hernia was repaired with fascia from the right thigh, and control biopsies of the skin and fascia lata were obtained. The skin contained 1.63 mg. and the fascia 0.20 mg. of ascorbic acid per 100 gm.

After 10 days, the healing skin and fascia scars were excised from the leg. A pigmented nevus on the same leg, but at some distance from the healing area, was also excised, with a margin of normal skin. The healing skin

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had an ascorbic acid content of 4.64 mg. per 100 gm., and the scar ruptured at a tension of 1600 gm. (average of four determinations). The fascia scar contained 6.79 mg. of ascorbic acid per 100 gm. and had a tensile strength of 1700 gm. The skin surrounding the small pigmented nevus showed a vitamin C level of 1.10 mg. per 100 gm. These results appear in Figure 9.

Discussion

We have attempted to obtain information concerning the importance of vitamin C in wound healing in human beings by means of tissue ascorbic acid determinations, contrasting the vitamin C content of ten-day-old healing scars in fascia and skin with that of control biopsies of these tissues obtained at the time the incisions were made. Direct tensile-strength determinations were also made on the healing fascia and skin scars.

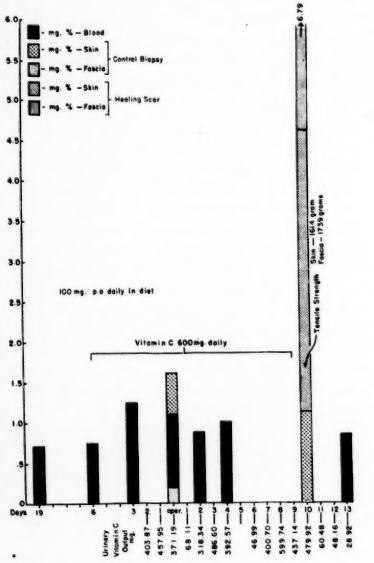

Figure 9. *Case 6.*

In the healing of an ordinary abdominal wound, the strength of the fascia layer is of primary value, and we are particularly interested in the results of the determinations on this tissue. These data have been assembled for convenient study in Table 1.

With the exception of Case 4, we believe that there is no significant variation in the behavior of the healing fascia in the cases reported. A comparable rise in ascorbic acid content and tensile strength is shown in spite of the variation in the preoperative plasma ascorbic acid from 0.20 to 1.19 mg. per 100 cc. In fact, in these 5 cases, the highest apparent tensile strength (2400 gm.) was found in the patient with the lowest preoperative plasma ascorbic acid (0.20 mg. per 100 cc.).

Except for Case 4, the ascorbic acid contents of the control biopsies of fascia were fairly consistent, varying from 0.11 to 0.48 mg. per 100 gm., with an average of 0.25 mg. Incidentally, this was considerably lower than the average vitamin C content of the control skin biopsies in these same patients, which was 1.35 mg. per 100 gm.

The healing fascia scar showed a marked rise in ascorbic acid content in every case, ranging from 3.88 to 7.65 mg. per 100 gm., with an average value of 6.01 mg. This is an average rise of more than twenty-four times the control level.

Table 1. *Studies on Healing of Human Fascia.*

Case No.	Preoperative Plasma Ascorbic Acid	Control Biopsy Tissue Ascorbic Acid	Ten-Day-Old Scar tissue ascorbic acid	tensile strength
	mg./100 cc.	*mg./100 gm.*	*mg./100 gm.*	*gm.*
1	0.63	0.29	3.88	1600
2	0.20	0.48	4.48	2400
3	0.29	0.11	7.65	1200
5	0.84	0.17	7.24	1100
6	1.19	0.20	6.79	1700
Average	0.63	0.25	6.01	1600
4 (first operation)	0.09	0.0	0.0	300
(second operation)	0.07	0.0	5.73	1800

The tensile strengths of these five specimens of fascia varied from 1100 to 2400 gm., and averaged 1600 gm.

We believe that the values obtained on these 5 patients can be considered normal, and in this group, even a plasma ascorbic acid level as low as 0.2 mg. per 100 cc. did not cause a significant variation from the normal in vitamin C content or tensile strength of the healing fascia.

Case 4 offers a contrasting picture, which we regard as significant, because the plasma ascorbic acid was very low preoperatively (0.08 and 0.09 mg. per 100 cc. on two determinations), and because the presence of bilateral inguinal hernias offered the opportunity for contrasting experiments in the same patient. The first leg wound was allowed to heal without vitamin C therapy, other than the 100-mg. daily dose provided in the regular diet. During the ten-day healing period of the second leg wound, this dietary intake was supplemented by 100 mg. of ascorbic acid daily given by mouth. The tissue ascorbic acid level of the control biopsy of fascia taken at the time of the first operation was zero. During the ten-day healing period of this wound, the low plasma as-

corbic acid level remained unchanged, and at the end of this time the excised fascia scar still showed an ascorbic acid value of zero and a tensile strength of only 300 gm., or about one fifth of normal (1600 gm.). The control biopsy of fascia from the second leg wound also showed a zero value for ascorbic acid. This wound was allowed to heal for ten days, 1000 mg. of ascorbic acid being given orally each day in addition to the regular diet. The plasma ascorbic acid promptly rose to over 1.0 mg. per 100 cc. At the end of ten days, the healing fascia scar was excised. Its ascorbic acid content was 5.73 mg. per 100 gm., which is slightly lower than the average of 6.01 mg. per 100 gm. noted in the other cases. The tensile strength of this fascia scar was 1800 gm., a figure slightly higher than the average of 1600 gm., for the other cases, and six times as high as that (300 gm.) for the scar in the wound in the other leg, which healed without benefit of vitamin C therapy.

The results of the studies of vitamin C content and tensile strength of skin healing appear in Table 2. These figures followed essentially the

TABLE 2. *Studies on Healing of Human Skin.*

Case No.	Preoperative Plasma Ascorbic Acid	Control Biopsy Tissue Ascorbic Acid	Ten-Day-Old Scar tissue ascorbic acid	Tensile strength
	mg./100 cc.	*mg./100 gm.*	*mg./100 gm.*	*gm.*
1	0.63	2.49	4.04	700
2	0.20	0.99	5.82	4200
3	0.29	0.84	5.23	1500
5	0.84	0.78	5.54	600
6	1.19	1.63	4.64	1600
Average	0.63	1.35	5.05	1700
4 (first operation)	0.09	0.0	0.67	400
(second operation)	0.07	0.0	6.77	1200

same pattern as those on the healing fascial scars, although there was much more variation in the tensile-strength determinations.

If we exclude Case 4 and accept the averages of the other 5 cases as normal values, we find an ascorbic acid content of the control skin biopsy of 1.35 mg. per 100 gm., which rose to 5.05 mg. in the ten-day-old scar. The average tensile strength of these scars was 1700 gm.

Case 4 showed an ascorbic acid level of zero in the control specimen of skin, which rose only to 0.67 mg. per 100 gm. after ten days of healing without vitamin C therapy other than the 100 mg. daily in the diet. The tensile strength of this scar was 400 gm., one quarter of the normal value. The second leg wound showed no vitamin C in the control skin biopsy. After ten days of intensive vitamin C therapy, the scar had an ascorbic acid content of 6.77 mg. per 100 gm., which is somewhat higher than the normal (5.05 mg.). Its tensile strength was 1200 gm., as against 400 gm. for the untreated scar in the same patient, and 1700 gm. for the average of the other cases.

We believe that Case 4 demonstrates conclusively two important points: that a sufficient depletion of vitamin C, reflected in a very low plasma ascorbic acid, interferes with normal wound healing, as measured by tissue ascorbic acid content and tensile strength; and that, in spite of a very low plasma ascorbic acid at the time of operation, normal wound healing can be brought about by adequate vitamin C therapy during the healing period.

There seems to be no evidence from these studies that a plasma ascorbic acid level of 0.20 mg. per 100 cc. indicates a sufficient depletion of vitamin C to interfere with normal wound healing, and this suggests that the generally accepted concept that plasma ascorbic acid levels below 0.50 mg. per 100 cc. indicate significant vitamin C depletion must be revised downward.

It was found in our work on guinea pigs that, with an adequate vitamin C intake, not only the tissues of the healing wound show a higher level of ascorbic acid than the control biopsy, but a similar though smaller rise is found in the abdominal wall at some distance from the wound. In 2 patients (Cases 5 and 6), specimens of skin were obtained at a distance from the healing wound at the time that the wound biopsy was done. As shown in Figures 8 and 9, one of these specimens showed a level of 1.88 mg. per 100 gm. in contrast to an original value of 0.78 mg. in the control biopsy, whereas the other showed a decrease from 1.63 mg. in the control biopsy to 1.10 mg. per 100 gm., in the normal skin excised ten days later.

CONCLUSIONS

A sufficient depletion of vitamin C produces a decreased ascorbic acid content and tensile strength in healing wounds in the skin and fascia of human beings.

A fasting plasma ascorbic acid level below 0.20 mg. per 100 cc. must be reached before these changes appear.

In the presence of adequate vitamin C, the magnitude of the rise in ascorbic acid content in healing fascial scars, compared with that of control biopsies, is much greater than that shown by healing skin scars.

In spite of a low plasma ascorbic acid level at the time of operation, normal wound healing may be produced by adequate vitamin C therapy during the postoperative period.

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THE SO-CALLED "COAGULATION DEFECT" IN MENSTRUAL BLOOD*

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(with the technical assistance of M. A. Adams and Harriet MacDonald)

BOSTON

THE fluidity of menstrual blood and its apparent failure to clot have been the subject of numerous investigations.[1-3] Although all observers agree on the existence of the phenomenon, there is little agreement concerning its cause. It has been with equal enthusiasm ascribed to an anticoagulant present in uterine cervical or vaginal secretions, to the removal or absence of one or more of the factors concerned with blood coagulation and to changes in the circulating blood. The existence of this form of incoagulable blood is of interest to the investigators of blood coagulation, since it represents a phenomenon that might possibly be explained in the light of the newer knowledge of the blood-coagulation reaction.

From a consideration of the theory of blood coagulation at present accepted in the United States, it appears that incoagulable blood may result from a deficiency of one or more of the plasma constituents concerned with coagulation,—calcium, prothrombin and fibrinogen,—or in a lack of the clot-promoting activity associated with the euglobulin fraction of plasma, which has been found to be markedly reduced in the blood of patients with hemophilia.[4] Incoagulability of menstrual blood might also result from the presence of some specific anticoagulant. This communication presents the results of investigations undertaken to determine which of these various factors are concerned with fluidity of menstrual blood.

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From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, the Department of Medicine, Harvard Medical School, and the New England Hospital for Women and Children.

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Methods

At the suggestion of Dr. George Van S. Smith, of the Fearing Research Laboratory, Free Hospital for Women, the collection of menstrual blood was made by the insertion of a rubber cup,¶ which acted as an occlusive pessary, high in the vagina. Collections were usually made for twelve-hour periods, after which the contents of the cups were transferred to blood bottles, examined for the presence of clots, and placed in a refrigerator. For certain purposes, collections were made occasionally for shorter periods. Ten samples of menstrual blood were collected in this manner from 5 healthy women.

The methods for studying the effect of menstrual blood on normal human and hemophilic blood were those previously described from this laboratory. The rabbit-brain thromboplastin used in the investigation was prepared by our modification of the method of Quick.[5] Thrombin was obtained from prothrombin, prepared by the method of Seegers et al.,[6] by the action of rabbit-brain thromboplastin.

For control experiments against menstrual blood, two well-known laboratory forms of incoagulable blood were used: citrated and defibrinated blood. In the experimental work reported below, the observations were carried out on the supernatant fluids after centrifuging, at 1500 r.p.m. for ten minutes, samples of citrated, defibrinated and menstrual blood. All observations were made in a constant-temperature water bath at 37.5°C. For the sake of brevity, one typical experiment on each phase of the investigation is given. The results in all were entirely similar.

Experimental Results

The presence of an anticoagulant in menstrual blood was investigated by the placing of 0.1 cc.

¶Commercially marketed under the trade name, Hycup.

of citrated, defibrinated and menstrual bloods in glass tubes and the addition of 2 cc. of fresh uncoagulated normal venous blood to each, with a proper control. Table 1 shows conclusively that no

TABLE 1. *The Effect of Samples of Citrated, Defibrinated and Menstrual Blood on the Coagulation Time of Normal Venous Blood.*

PREPARATION ADDED	COAGULATION TIME
	min.
None (control)	7
Citrated blood	7
Defibrinated blood	2
Menstrual blood	3

prolongation of the coagulation time of normal blood occurred as a result of the addition of any of the three preparations. With menstrual and defibrinated blood, there was indeed a shortening of the coagulation time of the normal blood. This indicates the presence of clot-promoting activity rather than that of an anticoagulant.

These observations were repeated, hemophilic blood being used in place of normal blood. The results are shown in Table 2. It will be observed

TABLE 2. *The Effect of Samples of Citrated, Defibrinated and Menstrual Blood on the Coagulation Time of Hemophilic Venous Blood.*

PREPARATION ADDED	COAGULATION TIME
	min.
None (control)	69
Citrated blood	12
Defibrinated blood	7
Menstrual blood	3

that again there was no prolongation, but a sharp diminution, of the coagulation time of the hemophilic blood. Menstrual blood has therefore an abundance of clot-promoting factor for hemophilic blood. Such an activity has been described as occurring in normal, cell-free, citrated plasma.[4] The data show that menstrual blood contains even more of this factor than citrated normal blood.

Since the presence of an anticoagulant could not be demonstrated in *any* of the samples of menstrual blood, observations were directed toward an attempt to discover whether one or more of the factors concerned in the blood-coagulation reaction were diminished or absent.

Total calcium determinations on menstrual blood were always within the normal limits obtaining for circulating venous blood. The data of Tables 1 and 2 indicate quite clearly that menstrual blood also contains sufficient clot-promoting activity to initiate blood coagulation in both normal and hemophilic blood. However, to establish beyond question that the fluidity of menstrual blood was not due to deficiency either of calcium or of thromboplastin, 0.1-cc. amounts of a solution containing 0.25 per cent calcium chloride, with and without the addition of a 0.1-cc. solution of rabbit-brain thromboplastin, were added to 0.1-cc. samples of citrated, of defibrinated and of menstrual blood in considerable excess (Table 3). It is evident that the addition of neither calcium nor both calcium and rabbit-brain thromboplastin caused clotting of the menstrual blood. In this respect, the menstrual blood resembled defibrinated blood. Following the addition of calcium and rabbit-brain thromboplastin to citrated blood, coagulation occurred in the normal time of twenty-

TABLE 3. *The Effect of Calcium Chloride and of Calcium and Thromboplastin Solutions on Samples of Citrated, Defibrinated and Menstrual Blood.*

TYPE OF BLOOD	SOLUTION ADDED	COAGULATION TIME
		sec.
Citrated	Calcium chloride	120
Defibrinated	Calcium chloride	No clot
Menstrual	Calcium chloride	No clot
Citrated	Calcium chloride and thromboplastin	25
Defibrinated	Calcium chloride and thromboplastin	No clot
Menstrual	Calcium chloride and thromboplastin	No clot

five seconds. By exclusion, a deficiency or absence of prothrombin or fibrinogen, or both, appears to be the cause of the fluidity of menstrual blood. This hypothesis was investigated by efforts to demonstrate fibrinogen in the menstrual fluid and, as shown below, by the addition of prothrombin and fibrinogen to the menstrual blood. The presence of fibrinogen could not be demonstrated in menstrual blood by any of the standard chemical procedures.

Table 4 shows that the addition of 0.1 cc. of thrombin to 0.1-cc. samples of menstrual and of

TABLE 4. *The Effect of Thrombin, Fibrinogen, and Prothrombin and Fibrinogen Solutions on Samples of Citrated, Defibrinated and Menstrual Blood.*

TYPE OF BLOOD	SOLUTION ADDED	COAGULATION TIME
		sec.
Citrated	Thrombin	3
Defibrinated	Thrombin	No clot
Menstrual	Thrombin	No clot
Citrated	Fibrinogen	No clot
Defibrinated	Fibrinogen	No clot
Menstrual	Fibrinogen	No clot
Citrated	Prothrombin and fibrinogen	360
Defibrinated	Prothrombin and fibrinogen	60
Menstrual	Prothrombin and fibrinogen	71

defibrinated blood preparation caused no coagulation. This indicated conclusively the absence of fibrinogen. However, the restoration of 0.1 cc. of fibrinogen alone was unsuccessful in causing 0.1-cc. samples of menstrual blood and of defibrinated blood to clot. No effect was expected with citrated blood, since a full quota of fibrinogen was

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present, as shown by clotting following the addition of thrombin. When, however, a mixture containing 0.1-cc. each of fibrinogen and prothrombin was added to 0.1-cc. samples of menstrual blood and of defibrinated blood, clotting occurred abruptly. The presence of the increased titer of clot-promoting substance in both menstrual and defibrinated blood caused the coagulation time, when excess fibrinogen and prothrombin were added, to fall below that of citrated blood.

Discussion

In their behavior toward thrombin, prothrombin and fibrinogen, the menstrual blood and the defibrinated blood, or serum, were strikingly similar. The observations indicate that the fluidity of menstrual blood is caused by the absence of both prothrombin and fibrinogen. Expressed in common language, it follows that menstrual fluid is blood that has already clotted, and that there is no "coagulation defect." Hence, menstrual blood is serum containing formed elements and epithelial debris.

A natural question arises. If menstrual blood has already clotted, where are the clots? It must be remembered that menstrual blood is slowly excreted and that much of the fibrin formed has had time to be subjected to lytic action. Only two of the samples of menstrual blood, however, showed any increased fibrinolytic power. The nonprotein nitrogen of menstrual blood was also not increased. Furthermore, it is known that the presence of small clots in normal menstrual exudates is common.[7-9] When menstrual flow is copious or abnormally increased, — that is, when there is a faster flow, — the presence of large clots is a characteristic finding. Examination of the menstrual-blood samples used in this investigation showed macroscopic clots in 3 cases.

One clinical application of these observations lies in the interdiction, by some surgeons, of operations during the menstrual period. We have been unable to demonstrate any change in the coagulability of the circulating blood during the menstrual period. This, together with the findings recorded, indicates that the fluidity of menstrual blood alone does not constitute a reasonable basis for postponing surgical operations to the intermenstrual period. However, patients who suffer from a true hemorrhagic diathesis during the menstrual period have been reported. In these rare cases, when the platelet count is low, operations should of course be deferred until this condition is remedied or absent.

It is interesting that Hippocrates[10] made studies on the menstrual blood of women three thousand years ago. He observed:

> The menstrual blood is thicker, redder, and flows more copiously about the middle period of the discharge than either at its commencement or termination. Its amount in health is about twenty ounces in two or three days, — the usual period, — although great diversity exists in this respect, depending on the constitution of the individual. *The blood which is discharged, is red like that of victims, and it coagulates promptly if the woman is in health* [italics ours].

Conclusions

From the evidence presented, it is apparent that menstrual blood is blood that has already clotted. There is therefore no true "coagulation defect," and menstrual blood is a suspension of the formed elements of blood and tissue debris in serum.

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BILE-DUCT RECONSTRUCTION WITH VITALLIUM TUBES*

Report of a Case

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STRICTURES of the common bile duct are almost invariably caused by an injury to the duct during some operation on the biliary tract. These surgical accidents carry in their train complications that are always serious and very frequently fatal, not only because of the accompanying obstruction and infection of the biliary tract, but also because of the dangers and frequent failures that accompany attempts at surgical repair.

The methods used for the surgical repair of bile-duct strictures and injuries have been slowly developed over the last quarter of a century. Plastic repair of the bile duct on the Heineke-Mikulicz principle is the simplest device available. End-to-end sutures of the duct, transplantation of external biliary fistulas, anastomosis of the duct with the gastrointestinal tract, and replacement of the duct by a rubber tube have all been used.

Plastic repair of the duct in simple strictures and anastomosis of the common hepatic duct to the stomach or duodenum in the more serious strictures have given the best results. Transplantation of external biliary fistulas has had but little success, and is now rarely used. Replacement of a portion of the common bile duct by a rubber tube is successful so long as the lumen of the tube remains free of bile salts. Usually, however, the bile salts produce changes in the rubber tube, and deposits in its lumen sufficient to cause obstruction of the flow of bile. I removed one rubber tube from the common duct seven years after

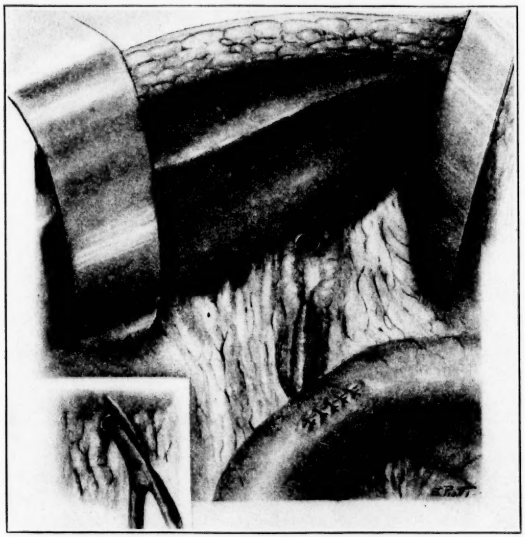

FIGURE 1.

The strictured area high in the common hepatic duct has been exposed. The opening in the duodenal wall, remaining from the previous anastomosis of the duodenum to the common bile duct, was first used for retrograde catheterization of the common duct and then closed. The insert shows the cutting of the fibrous ring about the opening of the common hepatic duct.

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it had been inserted. There was almost complete obstruction of its lumen by bile salts and detritus, and the rubber itself was friable and crumbly. I have also seen deposits of bile salts in the lumens of T tubes that had been in place but a few weeks. It is generally admitted, I believe, that rubber tubing does not offer a safe medium for use in repairing serious injuries to the common bile duct.

It occurred to Dr. Herman Pearse, of Rochester, New York, that a vitallium tube might be used

FIGURE 2.

The vitallium tube has been inserted into the stump of the common hepatic duct, being held in place with silk sutures. The distal portion of the common duct has been freed.

to replace or reconstruct an injured common bile duct. He[1] showed that bile made no changes in vitallium, and he has successfully implanted vitallium tubes in 2 cases of common-duct stricture. Through the kindness of Dr. Pearse, I was given an opportunity to employ this method in a very difficult common-duct stricture. Vitallium tubes of the required type, which differ in shape from the ones used by Dr. Pearse, were obtained.* The case is reported so that other surgeons may be familiar with the possibilities of vitallium tubes in bile-duct strictures.

CASE REPORT

Mrs. M. L. (2488), a 38-year-old woman, was admitted to the hospital on June 30, 1938. Cholecystectomy for gallstones had been performed elsewhere 16 months previously, and hemorrhage had occurred from the cystic artery. A clamp was hurriedly applied and left in place for 24 hours. It apparently included the cystic artery and the uppermost portion of the common hepatic duct in its grasp. The common duct was explored 4 months later, because of attacks of pain, fever, chills and jaundice. No stones were found. A stricture was discovered, but was considered inoperable.

At operation on July 27, 1939, I found a stricture, almost complete, very high in the common hepatic duct. The stricture was incised longitudinally, and a rubber T tube placed in it. The patient was well for 5 months with the tube in place. It was then accidentally pulled out. Soon after that, attacks of pain, chills, fever and jaundice recurred.

At operation on April 14, 1940, I exposed the strictured common duct with great difficulty. About 0.3 cm. of the common hepatic duct was present. The duodenum was freed, and a hepaticoduodenostomy was performed. A ring of fibrous tissue about the opening of the common hepatic duct made me fear that the new opening might contract and obstruct. After 6 or 7 months, this occurred, and the attacks of pain, chills, fever and jaundice returned.

On November 29, I again exposed the common-duct area, cutting the duodenum free from its anastomosis to the

FIGURE 3.

The vitallium tube has been placed in the common duct. It should be noted that a portion of the duct is completely lacking. Convenient fat tabs and omentum were used to cover the exposed tube.

common hepatic duct. The anastomosis had diminished to pin-point size. By means of an opening in the duodenum, a probe was inserted through the ampulla of Vater, and demonstrated the distal portion of the common duct. The duodenum was closed, and the common hepatic duct was dissected free as it lay in liver tissue (Fig. 1). Its opening was a ring of firm, fibrous scar tissue. In the hepatic ducts was much detritus, as well as many tiny

*Manufactured by the Austenal Laboratory, Incorporated, New York City.

black gallstones. The opening of this duct was enlarged so that the trumpet-shaped end of a vitallium tube could be inserted and held securely with silk sutures (Fig. 2). The distal end of the tube was placed in the distal portion of the common bile duct, about 2 cm. of which was absent. Omentum was brought in to surround the tube (Fig. 3). A jejunostomy was made for postoperative feeding. A drain was placed in the region of the anastomosis, but not close to it.

Recovery was entirely uneventful, the highest temperature being 99.4°F. 2 days after operation. The patient was entirely well for 6 months and then had one attack of pain and transient jaundice. This was followed by a small wound infection that quickly cleared up. X-ray examination at this time showed no evident change in the position of the tube (Fig. 4). No further attacks have occurred, and the patient appeared to be very well when last seen (March, 1942).

The technical difficulties in this case were only those of exposing both the common hepatic duct above and the common bile duct below, in a field in which the landmarks had been largely concealed by inflammatory tissue and adhesions following the previous operations. Placing the tube in the bile duct was not difficult, because the diameter chanced to be just right; furthermore,

FIGURE 4.

This x-ray film, taken some months postoperatively, shows the vitallium tube in the common bile duct and its relation to the barium-filled stomach.

the ring of fibrous tissue in the common hepatic duct held the trumpetlike proximal end of the tube firmly in place. It is noteworthy that the vitallium tube bridged a gap of about 2 cm. in the bile duct.

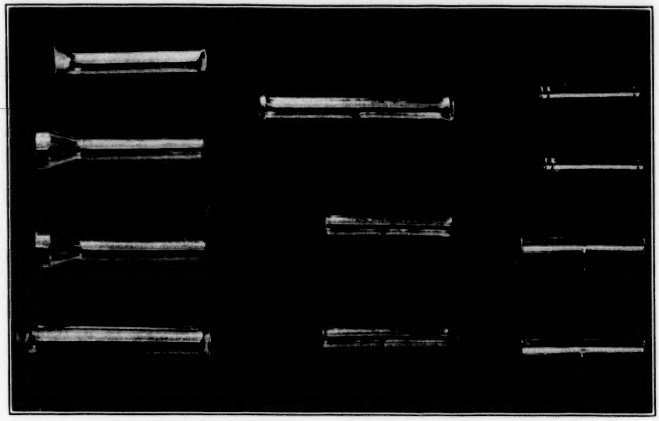

FIGURE 5. *Types of Vitallium Tubes for Bile-Duct Repair.*

Dr. Benjamin W. Seaman,[2] of Hempstead, New York, reports that his assistant, Dr. Carl Hettesheimer, has transplanted a vitallium tube into a strictured bile duct with success. An absence of about 2 cm. of the common duct was replaced. The patient was well nearly four months after operation.

It is apparent that in the future one must have various sizes and shapes of vitallium tubes at hand for the different-sized common ducts that may be encountered, although some alteration of the shape of the tubes can be made by cutting them with heavy scissors. In fact, it is now possible to obtain various shapes and sizes of tubes (Fig. 5).

I do not recommend that every case of stricture of the common bile duct be treated by implantation of a vitallium tube in the duct. I do believe, however, that such a tube can remain indefinitely in the body without being affected by the body fluids, and that increasing usefulness of such tubes will be evident. I am satisfied that, in the case reported, such a tube was of the greatest help to the surgeon, and a lifesaving device for the patient.

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Erratum

In the article, "The Treatment of Mammary Pain and Secretion with Testosterone Propionate," by Drs. Ira T. Nathanson, Joe V. Meigs and Langdon Parsons, which appeared in the February 26 issue of the *Journal*, the words "first" and "second" on page 324, column 2, lines 26 and 27, should be transposed.

MEDICAL PROGRESS

TRICHINOSIS AND ENTEROBIASIS: THEIR IMPORTANCE IN NEW ENGLAND*

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FROM a review of the literature, it is evident that trichinosis still remains the most frequent and the most serious of the parasitic infections in New England. It is also clear that enterobiasis, or pinworm infection, is probably second in frequency. Although the latter is definitely less serious than trichinosis, its incidence is such as to be of notable concern among pediatricians and public-health workers.

TRICHINOSIS

The extraordinary frequency of trichinosis in the United States began to be appreciated when Queen,[1] in 1931, briefly reported that examinations of diaphragms from 344 consecutive cases at autopsy in Rochester, New York, showed 59 (17.5 per cent) infected with trichinae, and that in a similar study made on 58 cases at autopsy in Boston, 16 (28 per cent) proved to be trichinous. Queen's data were in sharp contrast to earlier estimations, which placed the incidence of infection from 0.5 to 2.0 per cent for most civilized countries. Some inadequate data, however, did indicate a much higher rate of infection for some parts of the United States. These early figures were based on direct microscopic examination of relatively small bits of muscle, whereas Queen utilized artificial digestion of 50-gm. portions of the diaphragm in his cases.

Shortly after the announcement of Queen's findings, similar surveys were undertaken in nearly every section of the country. The results of these local studies have shown an astonishingly high incidence of trichinosis throughout the whole United States, ranging from 3.5 per cent in New Orleans[2] to 36.0 per cent in Cleveland.[3] These recent data do not indicate, as they at first suggested, that trichinosis has been rapidly increasing in this country or in any section of this country. On the contrary, the situation is probably improved in many localities over that of fifty years ago. It should be recalled, however, that within recent years two major epidemics of trichinosis have occurred within the New England states, namely, the Portland epidemic of 1935, which involved 71 persons, with 2 deaths,[4] and the epidemic among members of the Civilian Conservation Corps at Camp Charles M. Smith, Waterbury, Vermont, three years later, in which there were 64 cases but no deaths.[5]

Human trichinosis almost invariably has its source in pork infected with encapsulated larvae of the parasite. As an exception, attention repeatedly has been called to California outbreaks of the disease, which originated from eating jerked bear meat. Recently, a number of cases have been reported from Germany, following the eating of game and fur-bearing animals; in several cases, the infection originated from nutrias.[6]

Trichinosis in swine is usually the direct result of their eating raw trichinous pork, either in garbage or in offal at the time of slaughter. The primary source of rat trichinosis is, like that for swine, raw, infected pork scraps in garbage collected for swine, or in scraps picked up in the market districts or at abattoirs. Because of the high frequency or trichinosis in rats, it has long been held that rats are important reservoirs of infection for the disease in swine. Although swine may eat dead rats thrown to them, they are seldom known to kill and eat rats, even when they are numerous in hog pens. For the most part, rats and pigs seem to get along on quite friendly terms.[7-9]

The infection in rats may be considerably spread through cannibalism, but such infection probably is rarely transmitted to swine. Thus, human, porcine and rat trichinosis are all chiefly of porcine origin.

Since the young trichinae, the progeny of the adult male and female worms in the intestine, are passively carried to all parts of the body by the lymph and blood streams, the question early arose concerning the possibility of prenatal infection, as in ascariasis, hookworm infection and several other parasitic worm infections in which a blood-stream invasion is characteristic in the developmental cycle. Hood and Olson,[10] in 1939, found trichinae in four diaphragms from 48 infants under one year of age, and suggested that prenatal trichinosis might be a common occurrence. The weight

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, 1940* (Springfield, Illinois: Charles C Thomas Company, 1941. $4.00).

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of careful experimental evidence, however, fails to confirm this conjecture.[11–15]

The cause for the failure of *Trichinella spiralis* to produce prenatal infection is not known. However, the migrating larva is strikingly less active as a tissue borer than the larvae of helminths that are known to produce prenatal infection. It is deposited directly into the lymph stream by the gravid female worm in the intestinal wall. Subsequently, it is passively carried by the blood through the lung capillaries into the arterial circulation. Its main active migration occurs when it passes from the blood vessels and penetrates a muscle fiber. If this larva fails to penetrate a striated, skeletal muscle fiber, it is quickly surrounded by a focus of acute inflammatory exudate and is destroyed. This is known to be the fate of larvae that emigrate from the vessels situated in the heart, pancreas and brain; and although no trichinae have been found in placental tissues, there is every reason to believe that some are carried to the placenta, where they are probably as effectively destroyed as in other sites not favorable for encapsulation. It appears, therefore, that the sluggish nature of the larva, together with the acute and effective response of the host against larvae that fail to become encapsulated within the striated muscle fibers, may account for the freedom of the fetus from this parasite.

Recent studies continue to stress the irregularity of the clinical course of trichinosis, and to emphasize clinical aids in the diagnosis of sporadic cases. Kaufman,[16] from a critical study of 12 misdiagnosed cases of trichinosis, reported one clue, which, if heeded, would have suggested the correct diagnosis, namely, a history of puffy eyelids in the patient or in a member of the immediate family, or an edema of the eyelids at the time of physical examination. He suggests that in taking a history in all acute illnesses, one make specific inquiry concerning the presence of puffy eyelids, and that if there is such a history, or if they are observed at examination, the diagnosis be seriously considered. Andes, Green and Breazeale[17] and Lee[18] similarly note that edema about the eyes is one of the commonest symptoms, even in mild infections. McNaught[19] has recorded a new symptom in cases of active trichinosis: so-called "splinter hemorrhages," which occur beneath and along the distal ends of the fingernail and toenail beds and form a crescentic band of ecchymosis. This manifestation appears not to have been recorded heretofore, but according to McNaught it may be expected in 60 to 70 per cent of the cases of clinical trichinosis. It furnished strong supportive evidence in diagnosis during the recent epidemics in Wolverhampton, England.[18] These subungual hemorrhages occur at the time of invasion of the tissues by migrating larvae, and are of the nature of petechiae.

The presence of a blood eosinophilia, particularly a rapidly ascending eosinophilia, is generally held to be the most reliable sign of trichinosis.[16–20] The lack of an eosinophilia does not rule out the diagnosis, since this sign may be absent in severe fatal cases or in trichinosis complicated by a concurrent bacterial infection.[20, 21]

Laboratory procedures for demonstrating the presence of the parasite during the life of the patient have not been improved materially. Although migrating trichinae have been found in the blood and spinal fluid, young and encapsulated larvae in excised bits of skeletal muscle and adult worms and larvae in evacuated stools after drastic purgation, direct evidence of the parasite is usually not readily obtained.

Dammin[22] reports the ready finding of larvae in arterial blood from a case of trichinosis after unsuccessful examination of venous and capillary blood. He suggests the examination of arterial blood instead of venous blood.

For post-mortem examination, the compressor method and the combined digestion-Baermann method described by Nolan and Bozicevich[23] have been widely and successfully used. The first procedure consists in the compression of a 1-gm. sample of muscle, cut into small pieces between plate-glass slides, and examination with a low power of a dissecting microscope. The digestion-Baermann method utilizes the digestion of ground, striated muscle in artificial gastric juice; the diluted digestate is placed in a Baermann apparatus (used in hookworm studies for isolating infective hookworm larvae from soil samples), which is essentially a large funnel with a sieve that screens out the coarser particles and permits the trichinae to settle in the neck of the funnel. The compressor method has been particularly useful in detecting long-standing infections in which the trichinae are dead and calcified and would be missed with the digestion-Baermann method. The digestion-Baermann method has been used in the majority of the recent incidence studies.

Serologic and skin tests have been widely used for more than ten years. The results of observers who have had the most experience with these tests indicate that they are specific and of definite value as diagnostic aids.[5, 20, 24–28] In the experience of McNaught, Beard and Meyers,[28] the skin and precipitin tests have shown as high a degree of sensitivity as is found in any other clinical or laboratory procedure. However, limitations of these reactions for accurate diagnosis should be kept in mind. In view of the high percentage of people harboring the parasite, it is to be expected that some patients will give positive

reactions even though their illness may not be related to acute trichinosis. It was shown[29] and has recently been confirmed[30] that tissue and serum sensitivity to trichinella antigen may be present for years after a person has recovered from an attack of trichinosis. Thus, negative tests are more reliable in ruling out trichinosis than positive tests are in establishing the diagnosis.

Two types of skin reactions may develop in trichinous cases: delayed and immediate. The delayed reaction occurs during the first week of illness, and is similar to the delayed tuberculin reaction. After a second week, the skin reaction is immediate, consists of a blanched wheal surrounded by a zone of erythema, and gradually disappears about one hour after the antigen has been injected. The precipitin test does not become positive until about the fourth week of illness. It is especially useful if at first negative and later positive. For years, a chief objection to these tests was the difficulty in preparing or obtaining the antigen. At present, however, it can be obtained from at least two of the leading firms in this country that supply other biologic preparations.

A question of particular interest and one that is frequently raised in civil-court cases, is whether the patient suffers permanent injuries following recovery from acute trichinosis. Theiler, Augustine and Spink[29] elicited no residual symptoms from 7 patients seen from four to seven years after recovery. Warren, Drake and Hawkes[30] make no mention of any residual symptom in 45 patients examined three years after recovery from acute trichinosis.

The electrocardiographic findings of Spink[31] on 18 patients with trichinosis showed that myocardial damage, in recovered cases, is temporary. One of these patients, who showed marked signs of a weakened myocardium on the seventeenth day of illness, had a normal electrocardiogram thirty-two days later, the forty-ninth day after onset. Seven months later, the patient, on examination, complained of weakness, pain in the muscles of the extremities, dyspnea and palpitation on exertion, and slight edema of the ankles. The heart rate was regular, no murmurs were heard, and the blood pressure was 106 systolic, 70 diastolic. An electrocardiogram was normal. Beecher and Amidon[32] similarly reported only temporary cardiac damage in 44 cases of trichinosis followed by clinical and electrocardiographic examination.

Experimental evidence clearly supports these clinical deductions on myocardial injury in trichinosis. Graham,[33] in 1897, showed that myocarditis in trichinous rats is the direct result of the presence of young trichinae in the myocardium, although the muscle fiber is not penetrated. In Graham's experiments, the greatest number of larvae occurred in the heart muscle on the ninth day of infection, and very few larvae, if any, were definitely recognized after the fourteenth day. It therefore appeared that the developing trichinae either had been killed in situ or had left the myocardium by passing back into the circulation. Zoller[34] confirmed Graham's findings and expressed the belief that the injury to the heart muscle was only temporary. Dunlap and Weller,[35] studying the disease in white rats, found myocardial damage during the period of active dissemination of the trichinae, beginning as early as five days after infection, but it was not observed as soon as active migration of the larvae had ceased. No notable alteration of myocardiac tissue was found.

Most and Abeles[36] have contributed a comprehensive review of the literature relating to clinical manifestations and neuropathologic changes in trichinosis of the nervous system; they report 2 of their cases, 1 of which was fatal. The patient who on admission presented signs of mild, acute encephalitis made an uneventful recovery. Thirty-one days after admission, the neurologic and mental status of this patient was normal. From the review of the literature by Most and Abeles, it appears that no extensive damage to the nervous system is to be expected in trichinosis. Bercovitz[37] searched for residual symptoms of trichinosis in 70 patients recovered from one month to two years prior to his examination. He reported that of these patients, some of whom had suffered severely from the disease, 52, or 74 per cent, suffered no residual symptoms between one month and one year after recovery. Muscle weakness and muscle soreness were the chief complaints of the patients with symptoms, and these lasted for varying periods, but not longer than one year. In no case was there anything resembling a permanent disability.

From the information available, it appears evident that, at the most, vague muscle pains and ready fatigue may be expected to persist for some months after apparent recovery from trichinosis, but the repair of damage to the heart or other tissues in which the parasite does not successfully develop during the acute stage of illness is complete, and probably never results in a permanent disability.

In addition to the vast amount of study on the serologic reactions in trichinosis, there has been, during recent years, an ever-increasing interest in its immunity relations.

Without question, no other parasitic worm has so broad a host range as *T. spiralis*. Although the principal hosts, or the hosts most frequently

parasitized under natural conditions, are rats, swine and man, in all probability, any mammal can serve as a favorable host. In addition to these hosts, natural infections are now recorded in mice, domestic cats, palm civets, dogs, wolves, coyotes, foxes, pole cats, martins, ferrets, nutrias, European and American badgers, raccoons, polar bears, common bears and mongooses. Experimentally infected animals include guinea pigs, rabbits, hamsters, monkeys, sheep, cattle, gophers, horses, chickens, pigeons, magpies and rooks. Only young chickens are susceptible to muscular infection, which is of short duration.[38] Normal adult birds appear highly refractory to trichinosis, but muscle infection has been established in adult pigeons affected by avitaminosis.[39] Cold-blooded animals, fish and frogs appear to possess an absolute natural immunity against the parasite.[40, 41]

Recent investigations show that the diet of the host may significantly influence natural resistance to trichinosis. For example, McCoy[42] observed that young rats kept on a diet deficient in vitamin A are markedly more susceptible to the disease than those maintained on an adequate diet. The lowered resistance in the deficient rats was manifested by a persistence of the adult worms in the intestine, and also by the failure of these rats to develop any immunity against reinfection. Again, a diet lacking in vitamin E appears to enhance slightly the resistance of rats.[43]

It has been shown that animals that have recovered from an initial infection with *T. spiralis* resist reinfection.[44–46] When heavy doses of trichinae are fed to rats recovered from three or more sublethal infections, most of the trichinae are expelled after a few hours from the intestine.[47] Severe diarrhea is characteristic in reinfection in animals. It appears that the intestinal tract of the immune animal is "sensitized" following previous infection, and that the worms are thereby rapidly expelled on reinfection.[20] Whether recovery from an initial infection confers similar immunity in man is not known. It seems possible, however, that when the disease in man is marked by acute gastrointestinal symptoms and is not followed by other symptoms, the patient may have recovered from a previous infection.

Mauss[15] reported that the offspring of trichinous rats, rabbits and hamsters are less susceptible to trichinosis than the offspring of uninfected mothers. This lowered susceptibility is of short duration, being lost within about three weeks of birth. The transmission presumably occurs through the mother's milk.

Artificial immunity to *T. spiralis* has been produced by intraperitoneal injection of living larvae, of heat-killed larvae or of dried and powdered larvae.[48] The resistance induced by these methods is not so great as that brought about by active infection.

Conflicting results have been obtained from experiments on passive transfer of acquired immunity to trichinosis. Claims of beneficial results in acute cases of the disease in human beings by the use of serum from patients recovered from the infection[49] are not generally supported by animal experimentation. Culbertson and Kaplan[50] recorded passive immunization of mice by the injection of immune rabbit serum. The degree of resistance induced was very low. McCoy[48] obtained no evidence that immunity to trichinosis can be transferred passively by the use of serum from superinfected animals.

New light on the mechanism of immunity to trichinosis has been presented by Oliver-González.[51] According to him, two types of antibody appear in the serum of rats as a result of infection with *T. spiralis* — one acts specifically on the adult worms, and the other on the larvae. The former appears in the serum about the fifteenth day after infection, disappears by the fiftieth day and reaches its highest titer during repeated superinfection. By passive transfer, it partially protects rats against the intestinal stage of infection. In vitro, it causes precipitates at the mouth, anus and vulva of the female worms, and this is sometimes followed by death of the adult worms. The antilarval substance, which does not appear in the serum until about the thirtieth day after infection, reaches its highest titer about the fiftieth day after infection, but is not increased during repeated superinfections. In vitro, it causes oral, but no anal, precipitate, and sometimes death of the larvae. It gives little or no protection to rats against the intestinal stage of trichinosis.

From the results of Oliver-González's[51] studies, it is apparent that the varying results of earlier workers on passive transfer of acquired immunity to trichinosis may be attributed to the use of serums taken too long after infection, that is, at a time when the antibody content of the serum is low or absent and, particularly, in experimental studies, to the use of rats and guinea pigs, which, according to Oliver-González, do not produce such potent antibodies as rabbits do.

Experimental studies have failed to reveal a specific drug either for the removal of adult worms from the intestine or for the destruction of larvae in the blood stream and muscles. Results from the use of calcium lactate, parathormone, irradiated ergosterol and related substances forcing calcification of encapsulated trichinae in experimental animals do not warrant their use in the treatment of human infection.[52]

Although much has been written and said, little has been accomplished within recent years in the prevention and control of trichinosis. Until drastic changes are made in the methods of garbage disposal throughout the country, the only effective means of control must remain with the housekeeper, which means that all pork must be cooked thoroughly before it is eaten.

Enterobiasis

Enterobius vermicularis, the pinworm, is a parasite of human beings only. It occurs, in its various stages of development, from the lower ileum through the rectum. Unlike those of other intestinal worms, the eggs of the pinworm are not deposited in the intestinal tract. The gravid female worm characteristically migrates down the large intestine and through the rectum, especially at night, and lays her eggs on the perianal skin of the patient. The worms may travel a distance of several centimeters from the anus within an hour after the patient has retired.[53] Locomotion, however, ceases soon after exposure to the air. The eggs are then discharged by violent uterine contractions, and masses of eggs appear at the region of the vulva of the worm. The spent female worm then becomes shriveled and may drop from the body into the bed clothing.

Owing to this peculiar behavior of the female worm during oviposition, the usual methods of examination of feces for parasites are wholly inadequate and unreliable for detecting pinworm eggs. Thus far, the most reliable means of diagnosis has been the finding of the eggs collected in scrapings from the perianal skin. Several technics have been recommended for obtaining the eggs, such as the use of spoons, glass tubes and rods, spatulas and cotton pledgets, of which the first practical and efficient procedure was devised by Hall in 1937.[54] By Hall's method, the tip of a glass rod is covered with a square of cellophane held in place on the rod by a rubber band. The opposite end is carried through a rubber cork fitted into a glass tube, which prevents drying and loss of material during transportation and ensures safety of the carrier from infection. The swab has been generally referred to in the literature as the N. I. H. (National Institute of Health) swab.

To obtain a specimen for examination, the cellophaned end of the swab is passed radially among the perianal folds and over the neighboring perineum. Subsequently, the piece of cellophane, with the scrapings adhering to it, is removed from the glass rod and placed, face down, over two drops of physiologic saline solution, and examined under the microscope. In addition to the eggs of the parasite, vestiges of female worms or whole female worms may be present in the scrapings. Swabs should be taken during the night or in the morning before the patient bathes or defecates, preferably on at least seven days if the first results are negative.

Since the introduction of the N. I. H. swab, new studies on the incidence and epidemiology of enterobiasis have appeared in rapid succession. Cram[55] has summarized the results of various investigators on the incidence of pinworm infection, as revealed by the use of the N. I. H. swab, in the United States, Puerto Rico, Canada and the Philippines. Of a total of 22,376 persons examined, 9703, or 43 per cent, were positive. The distribution of positive cases is not spotted, as might be expected. The infection appears to be astoundingly high in the Boston area. Weller and Sorenson,[56] in 1941, in a clinical study of 505 white children, between the ages of two and twelve years, living in the Boston area, found 97, or 19.2 per cent, infected. In this group, 415 children were examined with one swab only. Of these, 74 cases, or 17.7 per cent, were positive. The remaining 90 cases were examined with two swabs. Of these, 23 cases, or 25.5 per cent, were positive. These later data illustrate the value of repeated swabs in diagnosis. It is probable that the findings of Weller and Sorenson may reflect quite well the frequency of pinworm infections in children throughout New England.

Recent studies have emphasized the familial nature of pinworm infection. Multiple cases are the rule rather than the exception, and frequently all the children of the family are infected, as well as one or both of the parents. Although families with pinworm infections are found most frequently in older, congested, residential sections, pinworm infections are not confined to any section or to any socioeconomic level.

Clinical symptoms in pinworm infection are exceedingly variable in both their nature and degree, being apparently absent in some cases and severe in others. The greater proportion of the cases studied by Weller and Sorenson[56] were essentially asymptomatic, although anal pruritus, skin lesions, enuresis, loss of appetite and masturbation were commoner in the children with pinworms than in those who did not have pinworms. Brady and Wright[57] noted gains in weight, improvement in color, disappearance of dark circles under the eyes, improved appetite and, particularly, improved social attitude and scholastic standing in many infected children after successful treatment. These authors did not find that enuresis, frequently attributed to pinworm infection, occurred with any greater frequency in their

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infected than in their noninfected group. It appears, however, that pinworm vaginitis occurs much more frequently than has been generally considered in the past. Of 45 cases in young girls examined by Brady and Wright, 14, or 31 per cent, were positive on one vulvar swab made at the introitus. Ten girls showed a mucoid vaginal discharge believed to be due to irritation of the genital tract from parasites migrating between the labia and into the vagina.

Africa[58] has summarized the literature on reported cases of enterobiasis in which pinworms migrated through the vagina and uterus into the fallopian tubes, causing symptoms of salpingitis, or into the peritoneal cavity, where they were found encapsulated in the peritoneum. He points to the fact that all such cases were observed accidentally during operation or at autopsy, which indicates that the condition may not be unusual, and that, obviously, many cases must have escaped notice.

The role of the pinworm in appendicitis is still an unsolved problem. Botsford, Hudson and Chamberlain[59] have expressed the opinion that the parasite may give rise to the syndrome of appendicitis without characteristic histologic changes. According to Chandler et al.,[60] it is only the fourth-stage larva of *E. vernicularis* that habitually burrows into mucous membranes, especially of the appendix, and there is a definite period six to nine days after infection when symptoms of invasion appear, followed four to seven days later by migrating worms from the anus. It appears, therefore, that the transient nature of the pinworm in the wall of the appendix may explain the many failures in demonstrating the worm at operation; because of these failures, the conception has become current that the parasite is not an important factor in appendicitis.

Wright, Brady and Bozicevich,[61] in 1938, recommended gentian violet for the treatment of enterobiasis; they obtained a cure rate of over 90 per cent, as indicated by the N. I. H. swab technic. The results of further tests on the specificity of the gentian violet for pinworms by D'Antoni and Sawitz,[62] Miller and his associates[63] and Wright and Brady[64] uphold the early results of Wright, Brady and Bozicevich. For adults, the recommended dose is 0.065 gm. (1 gr.) of the drug in a water-soluble, coated, four-hour type tablet given three times daily before meals for a period of eight days, followed by a seven-day rest period, after which treatment is repeated for eight additional days. For children, the recommended daily dosage is 0.01 gm. (⅙ gr.) for each year of apparent age. According to the authors cited above, the drug, in general, is well tolerated. Contraindications include concomitant Ascaris infection, any disease of the gastrointestinal tract, cardiac, hepatic or renal disease and pregnancy.

The control of pinworm infection is exceedingly difficult. The pinworm differs in its development from all other nematodes infecting man. The egg requires no prolonged period of incubation before it reaches the infective stage. When laid, the egg already contains an embryo, which becomes fully developed and infective on the skin of the patient within six hours. Infection is direct, that is, it follows ingestion of this egg.

During the last few years, particular attention has been given by investigators to the mechanism of pinworm infection. The infected patient may readily contaminate the hands while scratching the perianal regions to relieve itching caused by migrating worms, or when using the toilet. Pinworm eggs have been removed so frequently from under the fingernail that the examination of such scrapings has been advocated as a means of establishing the diagnosis. Sooner or later, the eggs on the hand are carried to the mouth of infected persons (autoinfection), or they may contaminate objects that can carry the infection to other persons. There is definite evidence that pinworm eggs may be carried about by air currents. Lentze[65] demonstrated experimentally that viable pinworm eggs could remain suspended in air for two minutes, and, on conclusion of the experiment, recovered eggs from his own nasal passages. Particularly important, at this time, are the epidemiologic studies on pinworm infection by Nolan and Reardon,[66] D'Antoni and Sawitz[62] and Sawitz, D'Antoni, Rhude and Lob.[67] Nolan and Reardon studied the distribution of pinworm eggs in household dust from seven homes, in each of which at least one member of the family was heavily infected. Viable eggs were found in dust taken from the floor and furniture and from the top molding of doorways and ceiling lights. Although the contamination of the furniture might have come directly from infected persons, the finding of viable eggs at the higher levels definitely points to air transportation. D'Antoni et al. obtained similar results from their study at six institutional homes for children. Viable eggs were found in all samples of dust collected in the dormitories from floor cracks, ledges of pillars of doors, windows and toilet partitions, at heights under eight feet from the floor. From these studies, it appears that the obstinate infection, which may persist for months or even years in spite of repeated anthelmintic treatment, is more probably the result of constant reinfection, frequently air borne,

than of an internal multiplication and development of the worms, as generally held in the past, but lacking confirmation.

Pinworm eggs are markedly resistant to physical and chemical agents. A temperature of 55°C. and above kills the eggs in a few seconds. At body temperature and on a damp base,—as on the human skin, especially under the fingernails,—they may survive for about ten days.[65]

Jones and Jacobs,[68] in a critical study on the survival of pinworm eggs under known conditions of temperature and humidity, found temperatures above 28°C., with humidities below 50 per cent, definitely destructive within twenty-four hours. None of the eggs survived after sixteen hours at a temperature of 36°C. and a relative humidity of 38 to 41 per cent. In water, at 3 to 5°C., the eggs survived for eighteen days. Ordinary disinfectants in strengths commonly used in the home do not kill pinworm eggs.

The futility of attempting to control pinworm infections in a household by hygienic measures alone was demonstrated in 1940 by D'Antoni et al.[62, 67] A vigorous cleanliness program was put into force for six weeks in a children's home that had been kept scrupulously clean. At the beginning of the experiment, extra housemaids cleaned every room with hot water and soap daily, and at night the children wore short cotton pants, which were changed and sterilized daily. Bed sheets were changed and sterilized daily, and underwear was changed daily and sent to the laundry. Nail brushes were provided for each child, and their use was enforced. Two showers were taken daily, instead of one. At the close of the experiment, swab examinations showed an increase from 38 to 51 per cent in the incidence of pinworms. In a similar home, treatment included prolonged use of gentian violet without special hygienic measures. Post-treatment swabs showed that a cure of approximately 90 per cent had been obtained.

Thus, hygienic measures alone appear to be of little value in the eradication of pinworm infection in the household, and control lies in simultaneous medical treatment administered to all infected persons within the household for a time sufficiently long to cover the period of survival of eggs in the surroundings.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28121

PRESENTATION OF CASE

First admission. A forty-four-year-old chauffeur was admitted to the hospital because of epigastric discomfort, chills and jaundice of about three days' duration, following a long story of related complaints.

Twenty-six years before entry, the patient was confined to bed for six months by an illness characterized by abdominal pain, jaundice, edema and passage of bloody stools. He had a temperature of 105°F. for one month, and subsequently lost his hair and desquamated extensively. Following recovery, he was well for a long time. Ten years before entry, he experienced an attack of "gas in the stomach," accompanied by jaundice, lasting two days. Seven years before entry, following breakfast, he developed a sharp midepigastric pain, which responded well to morphine given by a physician. Jaundice and fever followed, and the patient was therefore taken to a hospital, where roentgenograms were said to show an inflamed, stoneless gall bladder. While in that hospital, he suddenly "vomited bile," and was immediately relieved of his pain. After this episode, he had occasional spells of upper abdominal discomfort, sometimes followed by a yellowing of the scleras. He avoided fatty foods, on the advice of a physician. Four days before entry, he returned home from a trip in the country, feeling very tired. He noted slight epigastric discomfort, but this went away the next morning. This abnormal sensation, described as a "griping, uncomfortable feeling, not exactly a pain," reappeared in the afternoon. It did not radiate or extend from the midepigastrium. Again, it was relieved when the patient lay down to rest. That night, a mild chill occurred, followed by sweating. On the morning of the second day before entry, the griping sensation returned. The patient felt ill, and fasted. His physician found that he had a temperature of 101°F., that the scleras were jaundiced, and that the urine was "very dark orange." On the day preceding entry, the skin felt itchy, the jaundice was deeper, and the stools were clay colored.

On admission, the patient was mildly jaundiced. His general condition seemed good. There was slight tenderness in the epigastrium (positive Murphy's sign). The liver edge was just palpable. Examination of the heart and lungs was negative.

The temperature, pulse and respirations were normal. The blood pressure was 138 systolic, 98 diastolic.

Examination of the blood showed a white-cell count of 8700 with 75 per cent polymorphonuclears, and a red-cell count of 4,440,000 with 95 per cent hemoglobin. The hematocrit was 53.4 per cent. The blood sugar was 77 mg. per 100 cc., the chloride was 97.2 milliequiv. per liter, and the nonprotein nitrogen was 36 mg. per 100 cc. The van den Bergh reaction was biphasic, with a serum bilirubin of 9.2 mg. per 100 cc. The prothrombin time was normal.

The urine was normal, except for a + test for bile pigment. The stools were light brown, with a trace of bile pigment.

A roentgenogram of the gall bladder showed this organ to fill faintly with dye. There was no definite contraction after a fatty meal. The Graham test was considered positive.

On the fourth hospital day, duodenal drainage gave clear, dark green "A" and "C" specimens. No "B" bile could be obtained. After prolonged drainage, milky white bile was obtained from an uncertain locality. Crystals resembling calcium bilirubinate were found on microscopic examination of the bile obtained after the administration of magnesium sulfate.

The temperature continued to be normal. On the seventh hospital day, a laparotomy was performed. The liver appeared "diffusely scarred," suggesting "early cirrhosis." A large gall bladder, covered by tenuous omental adhesions, was removed. The common duct, dilated to a diameter of more than 2.5 cm., was opened, and freed of two pigment stones. The ampulla was subjected to dilatation and irrigation. A T tube was sutured into the common duct, and closure was effected, with drainage to subhepatic region. The pathological report was chronic cholecystitis and choledocholithiasis.

Postoperatively, there was elevation of temperature to 100°F., recurring for several days. Although considerable amounts of clear bile drained from the tube left in the common duct, the patient continued to be jaundiced. One week after operation, the serum bilirubin was 10.4 mg. per 100 cc., with a biphasic van den Bergh reaction. The blood chemical findings were otherwise essentially negative.

On the sixth postoperative day, roentgenograms showed that a Hippuran injection through the T tube filled the biliary tract well. The tract appeared distended. Two days later, a similar injection showed marked dilatation of the common duct, with two filling defects, suggesting stones,

at the lower end of this duct. There was extensive retrograde filling of the hepatic duct and of two irregular cavities in the liver suggesting abscesses.

By the twenty-fourth postoperative day, the serum bilirubin fell to 4.2 mg. per 100 cc., and there was only slight residual jaundice. The patient was discharged with the T tube still in place, draining an average of 300 cc. of bile a day.

Final admission (one month later). The patient had been followed in the Out Patient Department, and continued on "bile cocktails" and bile salts by mouth. Constant drainage from the tube was clear except on one occasion when there was a small amount of yellow granular sediment. After two weeks, drainage ceased, and the jaundice cleared entirely. Two weeks later, the tube came out of place during an examination with Hippuran, which showed the biliary tract still dilated, with no evidence of stones.

The patient was readmitted to the hospital because of sudden onset of vomiting and acute abdominal discomfort about four hours previously. After an hour and a half, the discomfort progressed to severe pain. During the next half hour, the patient had a severe chill. He vomited twice again, and was brought to the hospital.

On readmission, he again showed very slight jaundice. The scar of the laparotomy and drainage was well healed. The entire abdomen was distended, with tenderness and muscle spasm that were most marked in the right upper quadrant. Signs of peristalsis were absent. The heart and lungs were normal.

The temperature was 102°F., the pulse 130, and the respirations 18. The blood pressure was 140 systolic, 90 diastolic.

Examination of the blood showed a white-cell count of 13,600 with 88 per cent polymorphonuclears and 4 per cent band forms, and a red-cell count of 5,680,000 with 105 per cent hemoglobin. The urine showed a + test for albumin, and a ++ test for bile pigment. The stools were positive for bile pigment and for occult blood. A Miller–Abbott tube was passed as far as the pylorus, but could not be manipulated past this point. Clyses of glucose were given. The patient's temperature fell to normal, rising to 101°F. on the third hospital day. On the fourth hospital day, an operation was performed.

Differential Diagnosis

Dr. Arthur W. Allen: This is a long and complicated story. Is there anyone to demonstrate the x-ray films?

Dr. Tracy B. Mallory: We have the films, but no radiologist is here to interpret them. Perhaps Dr. Hamlin can help.

Dr. Allen: Where are the cavities that were thought to be abscesses?

Dr. Edward Hamlin, Jr.: There is tremendous dilatation of the entire biliary tree, especially the intrahepatic portion. The stones lie close to the ampulla. I was never certain about the abscesses.

Dr. Allen: Are they consistent with the size of the stones removed?

Dr. Hamlin: They are smaller.

Dr. Allen: At the age of eighteen, the patient had some very serious illness associated with fever and chills and jaundice that lasted for six months and during which his temperature for over a month was about 105°F. During this illness, he had edema, which might very well have been and probably was nutritional edema, because he had been ill a long while. Bloody stools were very probably the result of vitamin K deficiency, which accompanies jaundice of long duration. What that disease was, I do not know. Perhaps one can simply call it severe catarrhal jaundice, or hepatitis, and it probably was not associated with any mechanical obstruction to the extrahepatic ducts. It may have been some generalized disease affecting the liver secondarily. The patient apparently got along well for quite a while after this, and for sixteen years was without complaints. Then he began to have difficulty associated with gas on the stomach, and pain. The description is not too good, but it is probably good enough for me to say that ten years before admission the acute attack described was one of gallstone colic. The patient had indigestion and pain followed by jaundice. This responded well to morphine as pain of this sort does, in spite of all the scientific evidence that morphine causes a constriction of the papilla of Vater and therefore increases the pain and that one should use vasodilators instead. Every practitioner of medicine knows that morphine is the only drug that does these patients any good. The number of cases of the spasm type of pain that are relieved by antispasmodic drugs are very few, but the pain occasionally does respond to such medication, which, perhaps, should always be tried first. Usually, a real case of gallstone colic requires morphine for relief, and a large dose of morphine at that. The fact that this patient was suddenly relieved of pain when he vomited bile is interesting because, with the passage of a common-duct stone, the duodenum may suddenly be flooded with bile, which may be vomited. The morphine that was given for relief might have produced the nausea, but pressure within the common duct could account for it. I do not believe that we have to assume that the common duct perforated into the duodenum at that time, although this does rarely occur. The course was quite uneventful for nearly

seven years after that episode, with only occasional attacks of discomfort that a great many people with gallstones have and live with by dietary measures and accommodation of their mode of living.

Four days before admission, the patient had a strenuous time, apparently, following his trip in the country and began to have severe discomfort. Frequently, gallstone attacks are precipitated by motor trips. Any number of patients will tell you that such trips, as well as fatigue, produce an attack similar to that produced by indiscretion in diet. With the attack, this patient again had a chill, which began just before admission and which I suppose was the typical fever and chill of Charcot that is associated with inflammation in the bile ducts and is nearly always caused by stones.

The positive Murphy sign interested me. I asked a dozen or more students what the Murphy sign was; they did not know, and I meant to look it up but did not have time to do so. Apparently it is described here as tenderness in the epigastrium. I am familiar with Dever's sign, used by the late Dr. Charles A. Porter, which is associated with discomfort on heavy percussion over the right lower chest to indicate disease in or about the liver.

The blood count shows that the patient did not have very much infection at the time he was admitted. The Graham test was said to be positive, although no diagnosis of gallstones was made. The duodenal drainage is interesting in that crystals of calcium bilirubinate were obtained. We are not sure how reliable such a test is. When it is negative, one sometimes finds stones in the common duct, and when it is positive, one sometimes fails to find them. But when the experience has been accumulated, as it will eventually be, we can tell whether it is a 40 to 60 or a 30 to 70 chance. In this case, the test was positive, and stones were removed from the duct. The question arises about the white bile that was obtained and was said to be milky in appearance. It might be that the gall bladder was completely shut off by an old inflammatory constriction and that white bile was present within it. White bile rarely occurs in the common duct. We know that this man did not have a common duct full of white bile because they recovered green bile in the other two specimens. If this was white bile, it must have come from the gall bladder, and it was unusual that they could get it to drain, because one usually finds white bile when the cystic duct is completely occluded; this means that the bile has remained in the gall bladder long enough to have the pigment absorbed. How many weeks that takes, I do not know, but it probably takes quite a long while.

At operation, the liver was found diffusely scarred, suggesting early cirrhosis. I should think that any person who had been through what this man had twenty-six years before in the way of hepatic fever might very well be expected to have a liver that would appear grossly abnormal.

A large gall bladder covered with adhesions was removed. The record does not say whether the bladder contained white bile or not. The common duct was dilated to a diameter of more than 2.5 cm., a very large common duct, and two pigment stones were removed. We do not know whether these were irregular, very dark biliverdin stones, or bilirubinate stones, which are lighter in color, or yellow cholesterol stones. Perhaps it is not important, but I should expect that they were the biliverdin type because these are much more apt to get stuck in the common duct since they are so sharp, hard and irregular. The ampulla was dilated, and a T tube was placed in the common duct. If one has such a problem and finds that the common duct is 10 mm. in diameter, the right hepatic duct will be about 7 mm., and the left slightly smaller — about 5 mm.; therefore, if one is going to dilate the opening into the duodenum so that the stones can pass that have been pushed back or remain in the liver duct, — and I am sure this happens quite frequently, — one must gently stretch the outlet to a size slightly larger than the diameter of the right hepatic duct. One can measure the ducts accurately with instruments, and if one makes the outlet slightly larger than the right hepatic duct, stones that are overlooked are apt to pass through. We have collected stones from the stools in such cases.

At any rate, this man did well after the operation. The record mentions a fever of 100°F. for a while, and states that jaundice continued for a week or so and that the van den Bergh reaction was higher than that on admission. Decompression of the common duct does relieve jaundice, but it relieves it slowly. It takes just as many days or weeks for jaundice to clear up following decompression of the liver as it does for the patient to acquire the jaundice. If he has been jaundiced for three months, it will require about three months to lose all signs of icterus. This slow recovery does not bother me too much. Possibly, the fever and the increased van den Bergh reaction were indicative of a slight, temporary, acute hepatitis precipitated by this operative maneuver, and I think one might assume that such a hepatitis took place.

The Hippuran injection is interesting in that it shows beyond the T tube two opaque bodies

or areas that could very well be stones in the common duct. A great deal of work has been done on the Hippuran injection of the biliary tree, and many surgeons have advocated performing this test on the operating table. Dr. Charles G. Mixter, who has a good setup for such examinations at the Beth Israel Hospital, believes that it saves re-exploration of many ducts. Mirizzi,[1] of Cordoba, Argentina, has written an excellent monograph on this procedure; he describes many cases in which second operations have been avoided by Hippuran injection done before the patient left the operating table. Our experience in this procedure has not been particularly good. In one case recently,—in which we knew that the patient should have another stone, since we had counted them before and could not find the last one,—we did a Hippuran injection in the operating room; the x-ray plate showed the duct all clear, the dye going into the duodenum without incident, but a week later, when we repeated the test, there was the stone outlined beyond the T tube just as clearly as these two shadows shown here. The stone may hide itself in the liver ducts and then may come down with the current of bile without passing through the papilla of Vater. I suspect that is what took place in this case. It may be a mysterious and peculiar situation, but as the history is given, I believe that that is what this man had. I do not believe he had any of the bizarre or peculiar situations that sometimes produce symptoms and signs that are similar to those of common-duct stones.

I believe that the second admission was probably due to bile peritonitis. The patient had lost the T tube two weeks before he came back. His last illness was precipitated by a very sudden onset of discomfort, and on examination with the stethoscope he was found to have a silent abdomen. Since the T tube had come out of the duct and the external wound had thoroughly healed, one could visualize that, with stoppage in the common duct due to stone in the region of the papilla, the patient might well have opened up the old incision in the common duct and developed a bile peritonitis. It is obvious that intestinal obstruction was considered, because a Miller–Abbott tube was passed. It is quite possible that the patient had something else to explain this very acute upset that brought him back to the hospital, but it certainly suggests bile peritonitis.

Bile peritonitis is quite a dangerous condition, and in 18 cases that we have had in this hospital in a period of ten years, the mortality was 22 per cent.[2] That is lower than it is in most clinics. McLaughlin[3] has recently published an article on bile peritonitis and collected what he could from the literature on the subject. His mortality percentage ranged between 40 and 60 in various hospitals. In this clinic, it is low because we have learned that early recognition and early operation are indicated.

This man survived whatever this acute episode was for four days and was reoperated on; I should expect to hear that bile peritonitis was found at this operation and that very probably they were able to remove more stones from the common duct when they explored it.

DR. HAMLIN: I operated at the first operation. Dr. Allen has described exactly what the situation was, and the subsequent events. At operation we found a very large common duct. We could palpate the stone close to the ampulla. After we had opened the common duct, we explored the hepatic ducts before we took out the obvious stones, to obviate the loss of stones above. We found none. We took out the two stones, dilating the ampulla, but probably not enough. The patient seemed to be doing well until the illness described took place. I did not see him on the second admission, except when he was operated on, and at that time the surgeon opened into a large abscess cavity of bile peritonitis, which was apparently rather tightly walled off. The surgeon believed that the patient was too ill for the common duct to be explored at that time. Drains were put in the abscess cavity, and for two or three days he was quite well and his drainage decreased very much, although he did have some bile in the stools and in the intestinal contents. He finally developed a hepatorenal syndrome, and died in apparent renal failure.

DR. ALLEN: This is interesting because it is very difficult to prevent an external biliary fistula. An external fistula will break through the incision even if it is two or three weeks old, or bile will come through an old drainage tract, in almost every case. The Medical Service studied an interesting patient about six months ago: a woman who had had a cholecystectomy elsewhere shortly after delivery of her first child. She was about twenty-three years of age. She did badly after the operation and was re-explored in the hospital where she had had the original operation, and at this time they made a new incision. Both these incisions healed; the patient still did badly and after three months came to this hospital with a tremendously swollen abdomen. She had fluid in the abdomen, jaundice and a very high prothrombin level, and when they tapped her abdomen they obtained bile. When we explored her, we found that the common duct was communicating with a huge false sac, which filled almost the whole peritoneal cavity. We were able to pick up the proximal end

of the common duct and re-establish continuity with the intestinal tract. It is very unusual for anyone to survive confined bile leakage for such a long time. In every other case, in my experience, in which the patient has survived any length of time, bile has forced its way to the surface through the old drainage tract or through the incision.

Clinical Diagnosis

Common-duct stone, with obstruction and probable bile peritonitis.

Dr. Allen's Diagnoses

Choledocholithiasis.
Cholangitis.
Bile peritonitis.

Anatomical Diagnoses

Choledocholithiasis (intrahepatic).
Cholangiectasis.
Biliary cirrhosis.
Focal acute hepatitis.
Bile peritonitis.
Chronic pancreatitis, with fat necrosis.
Pulmonary infarcts, bilateral.
Icterus.
Bile nephrosis, slight.

Pathological Discussion

Dr. Mallory: At autopsy, an extensive bile peritonitis was found. We were unable to demonstrate any actual communication between the peritoneal cavity and the biliary-tract system. Undoubtedly, a fistula must have been present, but it had apparently more or less closed off and certainly was not widely patent at the time of autopsy. The common duct did not contain any stones. However, in the duodenum just beyond the papilla we found a stone that we may have forced out of the common duct in manipulating the tissues. In contrast, when we followed the ducts up into the liver, we found the biliary radicles enormously dilated, as one sees in the x-ray film, and many stones within them, more than a dozen. The remainder of the liver was scarred and tough, and showed an unusually severe grade of biliary cirrhosis. In fact, I cannot remember having seen a liver in which there was so much collagen surrounding the bile ducts. In a localized part of the liver, there was also acute infection of the smaller bile ducts, many polymorphonuclears and some organisms being visible in the sections. So that there was a localized acute hepatitis, as well as old chronic biliary cirrhosis, but no gross abscess.

It is interesting, when one considers the death from apparent uremia, that the kidneys showed virtually nothing. There was, as there always is, a slight degeneration of the tubules, so-called "bile nephrosis," which is invariable with chronic jaundice, but it is difficult to see how that per se would affect function of the kidney. I should be inclined to consider this primarily a case of liver failure rather than one of renal failure.

Dr. Allen: I wish someone would tell me what the disease was that the patient had at the age of eighteen when he was ill for six months.

Dr. Mallory: There was nothing at autopsy by which we could say. It is conceivable that it was cholecystitis and cholangitis even at that time, since the fibrosis within the liver was so extremely dense and old.

Dr. James A. Halsted: Do you think that it could have been typhoid fever, with localization in the gall bladder and subsequent formation of stones?

Dr. Mallory: That is conceivable. The gall bladder was not cultured at the time of the first operation.

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CASE 28122

Presentation of Case

A forty-six-year-old Greek leather worker was admitted to the hospital because of pain in the left knee.

The patient was well until nine months before entry, when he noted pain and swelling in his left knee that became gradually severer. The pain was most marked over the sides of the knee. There was little limitation of motion until two weeks before entry, when the knee became stiff, interfering with walking. There were no chills, fever or other symptoms, except slight malaise.

The past history was irrelevant. The patient had never had gonorrhea.

On admission, the patient appeared swarthy, heavy-set and in no acute distress. The left knee was swollen and hot. A mottled, brownish skin discoloration over the knee suggested previous application of heat. There was tenderness over the medial and lateral tibiofemoral fossas, more marked over the medial. The knee was held in 15 to 20° flexion, and only 5 to 10° more flexion was possible without extreme pain. The patella was not ballotable, but there was questionable fluctuation of the soft parts at each side of it. A lymph node 3 cm. in diameter was palpable in

the left groin, and one about 2 cm. in diameter in the right groin, neither being tender. There were no other positive physical findings.

The temperature was 99°F., the pulse 80, and the respirations 20. The blood pressure was 130 systolic, 90 diastolic.

Examination of the blood showed a red-cell count of 4,480,000 with 13.2 gm. hemoglobin, and a white-cell count of 5200 with 61 per cent polymorphonuclears. The blood Hinton reaction was negative on two occasions. The sedimentation rate was within normal limits. The urine was normal. A skin tuberculin test was performed, but the result was not recorded on the chart.

Roentgenograms of the left knee showed a finely granular area of calcification along the lateral margin of the right knee joint close to the region of the capsule, but extending downward and backward to the head of the fibula. There was indefinite follicular calcification just above the head of the fibula in the lateral view. There was a small amount of fluid in the upper recess of the knee joint. An area of diminished density I cm. in diameter appeared in the medial portion of the tibial eminence. No definite soft-tissue mass was seen.

Aspiration of the knee joint gave slightly cloudy, orange synovial fluid, with a viscosity of 9.9 and a normal mucin content. The fluid contained 11,550 red cells and 1150 white cells per cubic millimeter, with 6 per cent polymorphonuclears, 62 per cent monocytes, 22 per cent lymphocytes and 10 per cent clasmatocytes.

On the fifth hospital day, an operation was performed.

Differential Diagnosis

Dr. Claude E. Welch: It appears that stiffness of the knee rather than pain was the factor that brought this patient into the hospital. There is no mention of any previous inflammatory lesions, such as boils, that would suggest a secondary inflammatory lesion of the bone.

It is of some interest that no distinct mass was palpable.

It is interesting that the men in charge considered it unnecessary to do other blood chemical studies.

May we see the x-ray films?

Dr. George W. Holmes: I can point out only the things that are indicated in the text—the area of calcification and the soft-tissue changes described. Here is the area of diminished density in the region of the tibial tubercle. In the lateral view, this area is not visible. The area of increased density in the soft tissue seems to lie posterior to the head of the tibia and below the fat layer, in the muscular layer or in the margin of the capsule. It is important to know whether it is in the capsule or in the soft tissue just external to the capsule. I should say it was external, but that is a guess. In addition, there is some questionable thickening in the region just above the patella and a questionable increase in width of the joint space; this is suggestive of fluid, but there is no positive evidence of fluid. There is no bone atrophy, no evidence of spur formation about the condyles, nothing to suggest arthritis of the ordinary type, and nothing to suggest a chronic lesion like tuberculosis. So that from our point of view we have two things: an area of diminished density in the tibial tubercle, and an area of calcification in the soft tissues, neither of which I can explain.

Dr. Welch: I am interested that they term this spot "follicular calcification." Does that mean anything to you?

Dr. Holmes: It means that it was laid down in small flecks instead of masses.

Dr. Welch: I must admit that the findings of the aspirated knee-joint fluid mystified me, so that I asked one of our orthopedic experts about it. He said that he also was mystified, and we called the technician. I am not sure that I quote her correctly, but if I do, the fluid was thin, the normal mucin content being against arthritis. So far as the cell count is concerned, there is evidence against any type of septic joint, and that is as far as one is justified in going.

I shall mention the commonest lesions that may be expected in the knee joint and indicate the ones we can rule out. I have written them down in a more or less unclassified fashion. Could this be a metabolic disease, such as gout? There is no information, so far as the blood uric acid is concerned, and it is very unusual to have a single joint involved. Also, the history is not very typical. There were no severe paroxysms of pain. Could it be a Charcot's joint? Obviously not, according to the x-ray picture. Could it be tuberculosis? Dr. Holmes has remarked about the atypical features of the x-ray film so far as tuberculosis is concerned; clinically, this does not suggest a tuberculous joint, which usually appears in an old person and is very painful. Could it be any of the various specific forms of arthritis, such as infectious arthritis? That would be very unlikely, since the articular surface was essentially normal. Gonorrheal arthritis is excluded on the same basis. Could it be rheumatoid or hypertrophic arthritis of the joint? The x-ray picture is against it. We have nothing in the knee tap that would specifically suggest that diagnosis.

Could it be osteochondritis dissecans? I think we can eliminate that by the x-ray picture.

We are reduced, it seems to me, to two lesions: an inflammatory lesion of the nature of a Brodie's abscess that had not involved the knee joint, and some type of tumor located just below the synovial capsule. The calcification in the lateral margin of the knee joint, whether in the capsule or external to it, was there for a certain length of time,—no one knows how long,—and I do not believe that we have any definite right to say that this area of calcification is significant, although it is possible. Then, can we call this an inflammatory lesion or tumor? If inflammatory, it was an inflammatory lesion with no temperature, no elevated white-cell count, normal sedimentation rate, normal differential count and an aspirated fluid that is not compatible. In other words, I am definitely inclined against the diagnosis of an inflammatory lesion, and I am inclined toward the diagnosis of tumor.

Suppose it is a tumor, what lesions could simulate this x-ray picture? That again is extremely difficult, because the x-ray film is not typical of any one of them. Primary tumors in that location are limited to osteogenic sarcoma of some type or synovioma, a primary tumor of the knee joint. The picture is not typical of a metastatic lesion except for the destruction of bone. It is hard to explain the area of calcification along the lateral margin of the joint on the latter basis.

It may seem that I have talked myself out of everything, but I must go on record as making one diagnosis, and I shall say tumor of the knee joint. I do not care to be more specific concerning the type.

Dr. S. P. Sarris: We had quite a discussion about this patient. A great many people saw the x-ray films, and I discussed the case with almost everyone in the X-ray Department and several members of the orthopedic and surgical staffs. We were stumped for a diagnosis, and I operated on this patient with Dr. Otto E. Aufranc in the hope that between us we might be able to handle the surgical and orthopedic lesions of this area. I operated with the preoperative diagnosis of Brodie's abscess at the upper end of the tibia. We had previous x-ray films, and it seemed as if the area had increased since the first films were taken. Dr. Aufranc, I believe, favored the diagnosis of aseptic necrosis of bone. At operation, the knee joint was opened, and presented the strangest sight I have ever seen. It was packed with split-pea-sized pearly masses that were very firm but also elastic. Many of them were entirely free of attachment to any of the normal structures of the joint, whereas others were embedded in the synovia or attached to it by the pedicles. I estimated there was about 200 cc. of solid material. It was all removed, and a synovectomy was performed.

Figure 1. *Foci of Hyaline Cartilage Developing in the Synovia.*

Dr. William B. Breed: When you finished the operation, what was your diagnosis?

Dr. Sarris: At that point, we still did not know what it was. We called over the pathologist, Dr. Walter Bauer and a few others, and even

after seeing the knee joint open we still did not know what it was.

Clinical Diagnosis

Traumatic synovitis, left knee.

Dr. Welch's Diagnosis

Tumor of the knee joint, unspecified.

Anatomical Diagnosis

Chondromatous metaplasia of the synovia of the knee joint.

Pathological Discussion

Dr. Tracy B. Mallory: The joint, as Dr. Sarris has explained, was completely filled with gristly material that proved on microscopic examination to consist almost entirely of cartilage. The cartilaginous foci formed within the synovia, as one can see from the photomicrograph (Fig. 1). The synovial mesothelium is at the top of the picture, and one can see that immediately beneath it are multiple round masses of varying size, each of which is a little focus of hyaline cartilage. The deposits are of varying age, some of them obviously freshly formed, whereas others must have been present for a long time, since they are partially calcified. When these foci arise in the synovial villi, they hang by narrow pedicles into the joint cavity, frequently break off and become joint mice. They continue to contain living cartilage cells. We have had one other case of this sort. In another possibly related case, the synovia was entirely replaced by chondrosarcoma, so that I suspect the cartilage can and occasionally does degenerate into malignant tumor. I should term the process chondromatous metaplasia of the synovia. There does not seem to be a great deal written about the condition, although Jones* reported 19 cases in 1924 from the Mayo Clinic. Its etiology is entirely unknown.

A Physician: Are you surprised that the x-ray film did not show more?

Dr. Holmes: One would not expect it to.

A Physician: What is the prognosis?

Dr. Mallory: Perfectly favorable.

Dr. Holmes: How did you explain the area of diminished density?

Dr. Sarris: I was going to add that, at the time of the operation, there seemed to be a mass of these nodules pressed between the two joint surfaces overlying this area, and we interpreted it as aseptic necrosis from pressure atrophy.

Dr. Mallory: The only point on which the various consultants who saw this patient before operation agreed was that diagnosis was impossible without biopsy.

*Jones, H. T. Loose body formation in synovial osteochondromatosis with special reference to the etiology and pathology. *J. Bone & Joint Surg.* 22:407-458, 1924. The histogenesis of cartilage as shown in chondromatosis of the knee joint. *Ibid.* 9:310-314, 1927.

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NEW LAMPS FOR OLD

Shortly after John Brown's ill-fated raid on Harper's Ferry, Henry Thoreau, impressed by that gallant fiasco, felt the need of doing something about it, of allying himself with a cause, no matter how fantastic, in whose spirit he believed. Against the advice of friends, he hired a hall, announced a mass meeting, and delivered an address in which he advanced the theory that we as a nation had used up our inherited liberties. Just as our other inheritances may eventually become depleted through taxation, dispersion and poor investment, so today, according to Thoreau's theory, we may again be said to have exhausted our stock of passively acquired freedom.

The Civil War was a crusade to reaffirm a nation's belief in democracy — in the viability of the various bills of rights under which free people might live. This belief was reaffirmed in 1917, and is today once more undergoing a trial by ordeal. This trial, to which we have been subjected for the last decade and which has reached its crucial period, concerns the fitness of a free people to assume the obligations as well as to enjoy the benefits of their liberty.

Liberty, which is basically a spiritual thing, can be interpreted as a very material thing when no need for testing it has arisen. This shore was settled largely by people who sought spiritual liberty, who strove for it, and who passed it on to their descendants. As the rich resources of the land came to the surface, the acquisition of wealth that could be chemically assayed became a universal goal, and liberty came to be interpreted as the right to acquire that wealth in unlimited quantities.

This inherited liberty is in its turn being used up, and a present generation must find its own freedom, for it is surely losing the old. The scale on which material goods are being destroyed today, and the rate at which the wealth of capital is being consumed, must make us acutely aware that the end of our present system of utilizing liberty is in sight, and that the era of private exploitation is over.

The "American way of life" that we are now fighting for must have a very different meaning from that which can be so easily read into the words of this phrase. If by the American way of life we mean the exploitation of the land for individual gain, — a universal and perpetual tally-ho in the pursuit of a dollar of easy virtue, — the American way of life is not only indefensible but has already vanished around the corner. If, however, by the American way of life we mean the safeguarding to each of the opportunity to work out his own destiny, if we mean a personal and national adaptability that will see us through the profound changes that are to come, we are in a fair way to construct a new liberty for our own generation.

HOSPITAL FACILITIES

THE Bureau of the Census of the Department of Commerce has recently released what it describes as "the most widespread survey ever made of hospital bed facilities in the United States."[1] In the release, figures are given for the year 1939, and they seem to be largely interpreted in terms of the "minimum requirements for adequate medical service," as set up in 1933 by the Committee on the Costs of Medical Care. The figures are then broken down into three groups according to the total number of beds per population unit for each state. Thus, four states, including Massachusetts, and the District of Columbia are said to have good facilities, and eighteen states to have adequate facilities; the remaining twenty-six are classified as having inadequate facilities.

Just what the Bureau means by the "most widespread survey ever made" is not clear. Six months previously, the American Medical Association[2] released its annual register of hospitals, listing at least 1,304,628 beds and bassinets (against the Bureau's stated 1,282,785 beds). The Bureau's release is also vitiated by its failure to consider its subject qualitatively. The only criterion used is the ratio of beds to population, and on this alone it passes judgment that more than half the states have inadequate hospital facilities. The Bureau implies that 2000 more 170-bed hospitals are needed in this country. This may appear necessary to some politicians, but of greater fundamental importance is the need for improving existing hospital facilities, so that more of the present beds can be approved by the American College of Surgeons and by the Council on Medical Education and Hospitals of the American Medical Association. This would mean not only a great increase in laboratories and equipment, but an even greater increase in trained man and woman power. The lack of quality and efficiency in hospitals is even greater than the lack of beds, and is less easily remedied. Of the hospital beds investigated by the American Medical Association, only a half were in hospitals approved by the American College of Surgeons and only a third were in hospitals approved for internships, residencies and fellowships by the American Medical Association.

If the Bureau of the Census is going into these matters, it appears that professional advice should be employed. It, of all governmental departments, should be up to the sixteenth (1940) census by now. The subject is too important to be discussed in any but the most enlightened and up-to-date manner. There is a war to win before the Nation returns to the political connivances of 1939.

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OBITUARY

SOMA WEISS

1899 - 1942

Doctor Soma Weiss, Hersey Professor of the Theory and Practice of Physic at Harvard University and physician-in-chief of the Peter Bent Brigham Hospital, died suddenly on January 31, 1942, at his home in Cambridge, Massachusetts, aged forty-three years. Death was caused by a subarachnoid hemorrhage.

Doctor Weiss was born in Bestercze, Hungary, on January 27, 1899, and came to the United States in 1920. Early in life, he showed great interest in scientific research and, while attending the Royal Hungarian University in Budapest, received the appointment of demonstrator and research fellow in physiology and biochemistry. This interest in fundamental research continued in an uninterrupted manner. In 1920, he became an assistant in pharmacology at Cornell University, and during this period, he made fundamental observations on the mechanism of vomiting and the action of digitalis. In 1921, he received his Bachelor of Arts degree from Columbia University, and two years later, graduated from Cornell University Medical School. Following an internship at Bellevue Hospital, New York City, he joined the Department of Medicine of Harvard Medical School as a member of the staff of the Thorndike Memorial Laboratory of the Boston City Hospital, at first under the direction of Dr. Francis W. Peabody and later under that of Dr. George R. Minot. While associated with the Boston City Hospital, he became assistant director of the Thorndike Memorial Laboratory and, later, director of the Second and Fourth Medical Services and chief of the Fourth Medical Service. He remained there

until 1938, when he was appointed physician-in-chief to the Peter Bent Brigham Hospital and Hersey Professor of the Theory and Practice of Physic at Harvard University.

Doctor Weiss was a member of many medical and scientific societies, including the American Society for Clinical Investigation, Association of American Physicians, American Heart Association, American Academy of Arts and Sciences and American College of Physicians. He was a member of the Council on Pharmacy and Chemistry of the American Medical Association, and took an active interest in the Massachusetts Medical Society and in many problems concerned with national defense.

His interests in medicine were extremely broad, but he was especially well known for his work in cardiovascular disease and in clinical pharmacology and therapeutics. Starting with a study of the velocity of blood flow with Dr. Herrman L. Blumgart, he devoted his attention to such problems as hypertension, carotid-sinus disorders, syncope, shock, beriberi, heart disease and chronic pyelonephritis. Shortly before his death, he published, with Dr. Lewis Dexter, a monograph entitled *Toxemias of Pregnancy*. All his writings reflected his interest in seeking the truth, which led him into a careful and patient search for scientific facts concerning the problem at hand. He was always subjecting his ideas and thoughts to investigation and experiment. Problems that were constantly arising on the wards were transported to the laboratory for solution. "How" and "why" were two words that he used frequently in the discussion of medical problems.

He had a number of pupils who now hold important posts in academic medicine in this country and abroad. His guidance and stimulus were an invaluable asset to them.

Here was a man with a profound knowledge of medicine, a keen sense of humor and the courage of his convictions, combined with a great kindness and consideration of others. The memory of Soma Weiss and his achievements will always remain in our hearts and in the record of his short but striking and productive career. As Tennyson remarked, "Tho much is taken, much abides."

C. S. K.

MEDICAL EPONYM

De Musset Sign

The de Musset sign of aortic regurgitation was described, not by a physician, but by Paul de Musset (1804–1880), brother of the poet, in his *Biographie de Alfred de Musset; sa vie et ses oeuvres* [*Biography of Alfred de Musset: His life and his works*] (Paris, 1877). The following translation is from pages 274 and 275:

> The illness so well cared for by Sister Marcelline had left him with a troublesome tendency to affections of the chest. . . . We called the doctors twice during the course of the winter; they bled him too often.
>
> Whatever they may say, I am convinced that their lancets caused him irreparable harm. At breakfast one morning in March, I noticed that my brother's head was bobbing involuntarily with each pulse beat. He asked my mother and me why we were looking at him with such a startled air. We told him what we saw, and he said, "I did not think you could see it; but I will reassure you."
>
> He made some sort of pressure on his neck with his index finger and thumb, and in a moment his head stopped marking his pulse. "You see," he then said to us, "that this dreadful illness can be cured by simple and inexpensive means."
>
> We were reassured, being ignorant, for we had just observed the first symptom of a grave malady to which he was to succumb fifteen years later.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Case History: Ablatio placentae, associated with hysterectomy and followed by death

A twenty-four-year-old para III was admitted to the hospital with a diagnosis of ablatio placentae. The past history was irrelevant. The two previous pregnancies had been terminated by cesarean section, the reason for the first section not being known.

The patient had had no prenatal care except for one visit to a physician at the beginning of the eighth month. When nearly at term, she began to bleed and summoned her physician, who made the diagnosis of internal concealed hemorrhage and immediately sent her into the hospital. Her condition on arrival suggested severe intrauterine hemorrhage. The uterus was firm, the fetal heart was not audible, and the patient was not in labor. Soon after admission, the vagina was packed with gauze. External bleeding became profuse. Two thousand cubic centimeters of 10 per cent glucose was administered intravenously, and was followed by transfusions totaling 3000 cc. of citrated blood. In spite of these measures, external bleeding continued, and a laparotomy was performed seven hours after the patient entered the hospital. The fetus and uterus were removed. The day following operation, the patient became

edematous, developed edema of the lungs, and died, presumably of cardiac failure.

Comment. Inadequate prenatal care may have been responsible for this death. There is no record of the findings when the patient was seen once at the beginning of the eighth month. It is probable that had she been seen again after that visit, increased blood pressure and albuminuria would have been recognized. In view of the two previous cesarean sections, unless this patient was practically moribund when she entered the hospital, it is likely that a laparotomy immediately on entrance, preceded by transfusion, would have averted this catastrophe.

The generalized and pulmonary edema that appeared the day after operation may well have been caused by the tremendous amount of fluid that this patient had. If not, the edema and cardiac failure were due to the cardiac asthma so frequently seen in cases of toxic separation of the placenta. If the patient's condition on arrival was so serious that laparotomy was contraindicated and conservatism seemed the only intelligent treatment, the cervix as well as the vagina should have been packed and a Spanish windlass applied. This method should have been adopted only as a last resort, with the knowledge that rupture of the uterus from the previous cesarean sections was always possible.

The record does not state that the hysterectomy following the cesarean was necessitated by a uterus that would not contract. This does happen in patients with a completely separated placenta, and the only way to control the bleeding is to remove the uterus. On the other hand, if it is not imperative to remove the uterus in a patient in such poor condition, hysterectomy is certainly a more serious operation than cesarean section, and hence is contraindicated.

THE ROLE OF THE MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH IN CIVILIAN DEFENSE*

Recently, several persons have asked me what part the Massachusetts Department of Public Health plays in the National Defense Program. They went on to say that, although they have frequently read and heard about the plans of other agencies, they have rarely come across any mention of the Department of Public Health.

The answer to this is that the Department of Public Health, as part of its everyday duty, must always be prepared to deal with emergencies that may affect the public health, such as epidemics, floods and hurricanes. Being always prepared for emergencies, I suppose we have more or less taken it for granted that the public would realize our effective participation in the defense program.

Twice within the past ten years, we have been called on to function in times of disaster of natural origin. The flood of 1936 in the Connecticut and Merrimac valleys and the hurricane and flood of 1938 are still fresh within the memories of all of us, although their magnitude and importance pale when compared with the enormity of the present problem. In both emergencies, the facilities of the department were readily made available to the distressed areas. In general, it may be said that in the present crisis we shall function according to a state plan, which was drawn up after the flood of 1936 and revamped in 1940 to include all state and allied agencies that must be called on to render aid during any major emergency.

It can be considered that the Department of Public Health has two parts to play in the present defense effort. The first, and perhaps the more dramatic part, is our role in the State Emergency Plan. On receipt of official notification of a possible disaster, the specialized personnel in the Massachusetts Department of Public Health report for duty at their assigned stations. On this official notification, many of our workers will report to various armories throughout the State, where they will function in close co-operation with the State Guard and various local organizations. The department is providing for two first-aid rooms in the State House for the care of State House personnel in time of disaster.

Our principal problem is to maintain public-health practices at the highest possible level of efficiency, for it is in times of disaster that such practices are most seriously threatened. Our staff members, through the various armories, are readily available to render advice, guidance and assistance in the many public-health problems that may arise. For example, the engineers may be asked to assist in a matter concerned with water supplies or sewage disposal. Military catastrophes of one type or another are quite apt to have a damaging effect on water supplies and sewage-disposal systems. Modern sanitary engineering has been perfected and developed so that in our time typhoid fever and other intestinal infections have been reduced practically to a minimum. Any interference with these systems must be instantly coped with, and for this reason our state engineers have staffed their field personnel in even smaller districts than the other divisions have.

If pollution of a water supply should occur, engineers would be immediately on hand to assist the water boards and water companies in taking whatever steps are necessary to render the water supply safe. Emergency chlorine and chlorinator depots are distributed strategically throughout the State to supplement the reserves of local communities. Engineers and inspectors are ready to assist in obtaining specimens for laboratory examinations to ascertain whether or not the water supply is safe. We have obtained the co-operation of local laboratories for emergency examination of such specimens in case it is impossible to forward them to the departmental laboratory.

Similarly, the engineers, together with the co-operating local agencies, are prepared to remedy disruptions in the sewage systems, since these disruptions may result in the pollution of water supplies and consequently in the possible spread of disease.

Our district health officers will undoubtedly be asked to co-operate in ascertaining whether or not epidemic conditions exist or threaten, and, if so, how they can be brought under control. They may be asked to help in ruling out communicable diseases among possible evacuees, and frequently in emergencies are asked whether or not preventive inoculations of one type or another are indicated.

Our supervisor nurses will be available to local health departments and visiting nurse associations in meeting

*A "Green Lights to Health" broadcast given through Station WAAB by Dr. Paul J. Jakmauh on Saturday, January 17, and sponsored by the Public Education Committee of the Massachusetts Medical Society and the Massachusetts Department of Public Health.

the problems of carrying out a generalized program under extremely difficult conditions.

Our nutritionists will be acquainted with the whereabouts of reserve food supplies and are skilled in such things as emergency feedings and the mechanics of setting up canteens.

Food inspectors and sanitary officers are always in demand to pass on whether this food can be used or that food should be condemned. Laboratories are distributed throughout the State in such a way that it can be immediately learned whether or not milk or food has been endangered by possible contamination.

Our medical social workers will undoubtedly be asked to bring to bear their comprehensive knowledge of community resources and of how they can be marshaled to effect a solution in any particular emergency.

It can readily be seen that to have units established in certain key armories will facilitate bringing to any part of the State the entire services of the Department of Public Health with a minimum of delay. From time to time, it is possible that certain key individuals might be released from armory assignments to work with other agencies in meeting particular problems that may arise. We must remember, however, that the first duty of the department is to make it possible for state services to reach into all corners of the State. We cannot limit our plans to any particular city or district. Every possible effort is being expended for the closest co-operation between our personnel and the splendid and comprehensive program worked out for this particular emergency by the Committee on Public Safety. For example, our State district health officers, of whom there are eight and who act as the official representatives of the Commissioner in their districts, have been designated by the committee on public safety as regional directors for health. In this respect, they have been of assistance in the formation of many local city or town committees, and have also assisted such committees in developing the desired program.

Our division directors keep in close touch with the policies and plans of the various subcommittees of the Massachusetts Committee on Public Safety, particularly those dealing with health and sanitation. In this way, the activities of our specialized personnel can be correlated and integrated with those of the state committees. Other members of our department are working in conjunction with the aforementioned committees on such things as emergency housing, evacuation hospitals and similar problems.

What I have said thus far constitutes our first role in national defense. I should like to dwell a few moments on our second role, which, although it may be less dramatic, is nonetheless significant. The so-called "home front" is always of importance in war, but particularly is this true at the present time. It is universally admitted that a continued uninterrupted flow of ships, tanks, planes and guns from the shipyards, arsenals and factories is an absolute necessity in the successful conduct of this war. That this stress of production may be uninterrupted, the public health must be kept at an unusually high level. It is at times such as this, when all are more or less overfatigued and continually busy about other things, that health may be allowed to become impaired. We must be on our guard to keep "sound minds in sound bodies." The children of today are the men of tomorrow, and the men of tomorrow are quite apt to be soldiers. We must profit by the lessons learned in the recent draft and put into effect all possible measures that will cause young men to appear before the Selective Service boards in the best physical condition. Similarly, the health of workers in industry must be protected and preserved, lest fatigue, malnutrition, respiratory disease or other disease be allowed to decimate industrial ranks and seriously interfere with production.

During the anxious days ahead, we must continue to throw every protection and safeguard about women and children. From a health point of view, no effort must be relaxed toward keeping our communities safe. Health-education measures designed to promote better nutrition must go on. The conditions of war, overcrowding, hunger and exposure, although fortunately not prevalent in this state, must be anticipated. Such conditions are the forerunners of epidemics. Because disease itself is absent from our midst at the present time does not mean that the bacterial causes are not always present, awaiting only suitable soil.

The second role that the Department of Public Health plays, then, is this critical one of making absolutely certain that the ground gained in the war against disease is not lost in the present crisis. Even though we were absolutely safe from bombing and sabotage, I should consider this maintaining of the public health to be an extremely vital assignment. This is, of course, not the responsibility of the Department of Public Health alone. Each local board of health is alert to the responsibilities, and plans to carry on in the future as in the past. The voluntary agencies are likewise mindful of their responsibility, and I can assure you that through the co-operative effort of all concerned, health standards will be maintained.

I shall now summarize briefly the dual role of the Massachusetts Department of Public Health in national defense. In the first place, it is prepared to bring to bear in any affected area in the State specialized personnel equipped and capable to cope with any situation. Such personnel will function out of certain key armories in close co-operation with the State Guard, local civilian-defense committees and local health departments. Secondly, it is alert to the need of maintaining health standards even in the absence of air raids and sabotage, and is gearing its efforts to cope with this very real, if less dramatic, duty.

DEATH

LADD — MAYNARD LADD, M.D., formerly of Boston, died March 9. He was in his seventieth year.

Born in Romeo, Michigan, Dr. Ladd received his degree from Harvard Medical School in 1898. He was formerly a member of the faculty of Harvard Medical School, director of the preventive clinic at Boston City Hospital, chief of the children's department of the Boston Dispensary and president of the American Pediatric Society.

He is survived by two daughters.

WAR ACTIVITIES

CIVILIAN DEFENSE

NURSING SERVICE FOR THE WAR

Nursing service is being rapidly organized to take its place in the civilian-defense program. A full-time nursing consultant is on duty as a member of the staff of the Medical Division of the Office of Civilian Defense in Washington, and the Subcommittee on Nursing of the

Health and Medical Committee of the Office of Defense Health and Welfare Services also serves as the Nursing Advisory Committee of the Office of Civilian Defense. Through the consultant and the advisory committee, the Medical Division is in contact with all federal agencies that have nursing programs and the Nursing Council on National Defense, which represents national nursing organizations, the Red Cross and federal agencies. To assist the regional civilian-defense offices in interpreting the emergency medical-service program, field nursing consultants of the United States Public Health Service, the United States Children's Bureau and the American Red Cross have been made available for consultation. One nurse representing the Red Cross and another representing one of the other two agencies have been assigned to each state.

The most recent development in the nursing program is the establishment of state nursing councils. These councils are made up of representatives of nursing organizations, official agencies with nursing programs and the Red Cross. It has been recommended by the Medical Division of the Office of Civilian Defense that the services of these state councils be made available to state defense organizations.

Nursing representation on local medical advisory councils has also been recommended by the Medical Division of the Office of Civilian Defense, and local nursing councils are being formed throughout the country.

Nurses are required in the emergency medical service now being developed by the Medical Division of the Office of Civilian Defense. They will be needed not only for the care of casualties in hospitals but for service with medical first-aid posts. If it is necessary to discharge patients from hospitals earlier than usual to make room for war casualties, nursing service may be necessary for such patients in their homes. For this purpose, the organizations in the community having public-health nurses will co-operate in meeting the needs for providing home care. Nurses will also be required for service in base hospitals, to be established in protected rural areas if needed for the reception of civilian casualties due to enemy action.

Other phases of the work of nurses in civilian defense are the training programs now being carried out in collaboration with the Red Cross. Both the Office of Civilian Defense and the Red Cross are urging promotion of the nurses'-aide program. One hundred thousand must be trained in the next few months to assist nurses in casualty receiving hospitals and in field casualty services. Nurses are being urged by the Medical Division to arrange to teach home-nursing courses, so that more women will be ready to care for sickness in their own homes during an emergency and relieve the hospitals of some of their load. Nurses are also asked to take Red Cross first-aid courses so that they may be prepared to help in casualty services and also to qualify as instructors for first-aid courses.

CORRESPONDENCE

"PSYCHIATRIC ASPECTS OF ULCERATIVE COLITIS"

To the Editor: "Psychiatric Aspects of Ulcerative Colitis," by Dr. George E. Daniels, in the January 29 issue of the *Journal*, is to my mind at variance with clinical experience and observation at the bedside. The influence of the nervous system on functional and organic somatic disturbances is not a recent psychiatric discovery. It has been known for decades that certain psychic and emotional states are the sole cause of general and local functional disorders, and quite often exciting causes in organic affections. An emotional upset quite frequently precipitates an attack or intensifies the symptoms of gallstone colic or of angina pectoris. In the latter condition, it is as potent a factor as physical exertion. But the essential causes of these diseases are the structural changes in the organs, and very few physicians would view them as psychiatric in origin. The same holds true regarding ulcerative colitis.

Mucous colitis is a comparatively rare affection, and spastic colitis, — or more accurately, a spastic colon, for there is hardly any colitis in this condition, — a very common one; whereas ulcerative colitis is less frequent than the spastic colon and much more frequent than mucous colitis. Ulcerative colitis begins rather suddenly with blood and bloody mucus in the stools; in some cases, it is preceded for a week or more by rather intense diarrhea, but in no case to my knowledge has there been any antecedence either of mucous colitis or of a spastic colon.

Ulcerative colitis is a chronic disease characterized by remissions and acute exacerbations, the remissions lasting from weeks to years. Patients with this affection have financial, economic and social worries and conflicts just as well as people with a normal colon. These worries and conflicts may be factors in acute exacerbations, but their absence, in my experience, is no factor in the remissions, which are due to the natural course of the disease and not to any psychiatric treatment per se. The personality of patients with this affection is, to my mind, about the same as that of persons with any other bodily disease or that of what we call normal people, although some colitis patients may well belong to the "giver-uppers." When a patient has about twelve to thirty evacuations, and rather painful ones, in twenty-four hours, one would hardly expect him to be jovial and optimistic, and it would be rather surprising if he should not eventually become a "giver-upper." Some clinicians maintain that there is no difference between the functional and the organic, and this is perhaps theoretically true. The concept of body-mind has a strong philosophic appeal, but the dualism of body and mind is eminently pragmatic, and there is at least some difference between multiple sclerosis and psychoneurosis accompanied by various organic disorders.

Ulcerative colitis is a severe organic disease characterized by remissions and exacerbations. Mental and emotional factors are of importance in its symptomatology, as they are in any other organic disease, but as to its being psychiatric in origin and pathogenesis, this view, to my mind, is purely scholastic and a return to medieval mysticism.

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SEROLOGIC TESTS FOR SYPHILIS

To the Editor: The necessity of serologic tests for syphilis as part of the examination of applicants for marriage licenses and the short time usually available to such applicants as are in military service is not infrequently subjecting the Wassermann Laboratory of this department to adverse criticism. We believe that a statement of the circumstances should demonstrate that such criticism is unjustified.

The performance of serologic tests for syphilis in a nonroutine manner, as is frequently requested for premarital examinations, is not feasible under the present laboratory setup. The very large number of routine tests (upward of 40,000 in January) throws such a burden on the facilities and personnel of the laboratory that it is not practicable to impose the additional burden of accepting specimens out of turn and testing them by nonroutine methods. Furthermore, it is unfair to accept such specimens at all unless the practice can be made general, and our physical facilities do not permit of expansion to carry such an added burden.

The rendering of reports by telephone, which is also requested frequently, would appear to be barred by the provisions of Section 119 of Chapter 111 of the General Laws, which provides that ". . . laboratory . . . records pertaining to gonorrhea or syphilis shall not be public records, and the contents thereof shall not be divulged by any person having charge of or access to the same, except upon proper judicial order or to a person whose official duties, in the opinion of the commissioner, entitle him to receive information contained therein." As the purpose of this statute is to protect the individual, and as the laboratory has no way to identify the source of telephone calls, it would seem that reports can be sent to physicians only by mail or by a duly accredited messenger.

Authorization to perform premarital examinations was granted to medical officers of the United States Army, Navy and Public Health Service on active duty by Chapter 697 of the Acts of 1941; and all Army, Navy, Public Health Service and state health department laboratories were approved by the Public Health Council for the performance of the necessary serologic tests. It is suggested that physicians call these provisions to the attention of the prospective brides of men in military service, so that the latter will not delay their own examinations needlessly.

In further recognition of the fact that many times the circumstances of military service and so forth give applicants for marriage licenses only a short time in which to fulfill the requirements of the law, we have inquired of all laboratories approved for performing serologic tests for syphilis as to whether they wish to accept such specimens for rapid testing and what their fees are for such services. This information has been tabulated in the hope that it will prove of service to physicians.

The following laboratories will do rapid Hinton tests (and confirmatory tests when needed) for premarital purposes, at the charge indicated:

Boston Dispensary	$3.00
Boston Health Department (Boston residents, only)	No charge
Brockton Health Department	
Brockton residents	No charge
Nonresidents of Brockton or nonresident physicians	$3.00
Leary Laboratory, Boston	3.00
Massachusetts General Hospital	3.00
Mercy Hospital, Springfield	2.00
Peter Bent Brigham Hospital, Boston	3.00
Providence Hospital, Holyoke	2.00
St. Luke's Hospital, Pittsfield	1.00

PAUL J. JAKMAUH, M.D.
Commissioner of Public Health

State House
Boston

REPORTS OF MEETINGS

HARVARD MEDICAL SOCIETY

A regular meeting of the Harvard Medical Society was held at the Peter Bent Brigham Hospital on November 12, with Dr. Elliott C. Cutler presiding.

The case presented was that of a seventy-three-year-old man admitted after an alleged injury in an automobile accident. When first seen, the patient appeared to be in shock but was mentally clear, with a blood pressure of 90/60. He was given emergency treatment for shock. Physical examination revealed mobility and crepitus of the pelvic bones, an obvious fracture and tearing of all the ligaments of the right ankle, and a sprain of the right knee; neurologic examination was negative. After an hour, the chart showed that the general condition was good, and the patient was removed to the operating room, where, under Pentothal anesthesia, the fractures were reduced. Again, the blood pressure fell, and he was given intravenous saline solution, 25 gm. of human albumin and a small blood transfusion. Hematocrit readings were taken at the time and subsequently as an aid in following the course of the patient. The later course was essentially smooth except for an anemia, for which he received further transfusions.

In discussing the case, Dr. Carl Walter emphasized the age of the patient, the fractures of the leg and pelvis and the element of shock. The early treatment of the fractures and the shock is an aid toward a favorable outcome, especially in aged patients. In all fractures of the pelvis, the question of bladder injury arises, but there was no evidence of any in this case.

The speaker of the evening was Mr. Gordon Gordon-Taylor, surgeon to Middlesex Hospital, London, and Surgeon Rear Admiral to His Majesty's Navy, whose subject was "Certain Surgical Problems of Modern Warfare." Slides were shown of the building of the Royal College of Surgeons before and after the bombing of May 10 and 11 of this year, when such damage was done that the collection in the Hunterian Museum was reduced from 14,000 to 3800 specimens.

The characteristic feature of the wounds in World War II has been their multiplicity — to an even greater extent than in World War I. Blast wounds have been common, and small fragments of glass or other debris often enter the superficial tissues. The best form of treatment in such cases is to paint the wounds with 1 per cent gentian violet or some other weak antiseptic and allow the foreign bodies to extrude themselves. This usually takes place without complication on about the tenth day.

The great paucity of gas gangrene as compared with 1914–1918 may be attributable either to the use of the sulfonamide group of drugs or to the plaster method of treating compound fractures. The incidence has been less than 1 per cent. The wounds were undoubtedly as well cleaned and débrided in the last war, and gas-bacillus antiserum is being employed only in wounds that involve regions known to predispose to gas infection, such as the buttocks, perineum, calves and inner thighs. This type of infection is certainly not unknown in the Navy, as was formerly taught, but is much less common.

Whether the type of injury is responsible is not certain, but secondary hemorrhage — the bugbear of the base hospital during the last war — is almost unknown. Similarly, traumatic aneurysm has become much rarer.

In wounds of the face and jaws, wide excision of tissue is almost never necessary, for the blood supply is

excellent and gas gangrene is very rare. Immediate suture is carried out if possible. Dependent drainage in fractures of the jaw is probably the most important single procedure. Whenever possible, the mucous membrane should be sutured immediately.

In the management of burns, there has been a recent trend away from the use of tannic and other eschars, especially on the face and hands, where early motion is a desirable factor. There seems to be little question that an eschar of some sort is necessary to save lives in widespread burns, but there is no unanimity of opinion regarding the face and hands. There are advocates for wet saline dressings, *tulle gras* and certain ointments.

The most frequent injuries sustained in the naval forces are those associated with mine explosions, which usually involve small commercial vessels or mine sweepers. The force is borne in the long axis of the body. Fractures of the os calcis and, to a less extent, the astragalus are most frequently seen. As might be expected, there is a high incidence of fracture of the lumbar spine in these casualties. Also encountered are fractures around the knee, of the femur and of the tibia, particularly the so-called "bumper type."

Injuries to the chest are of the same severity and frequency as those during the last war, but the treatment differs in that the wounds are usually drained for the first two or three days instead of being closed tight and subsequently aspirated. Together with abdominal wounds, they are the most infrequently seen, at least in the hospitals, possibly because such a large percentage of these patients die almost immediately. The same general rule holds in naval surgery: namely, that men hit in the trunk invariably die. In abdominal wounds, a complete examination is especially necessary, for there is often a very small wound of entry causing considerable internal damage. Wounds of the buttock are particularly prone to involve the peritoneal cavity, and one should always treat them with that possibility in mind. In general, if wounds of entrance and exit are found in both rectus muscles, one can be fairly certain that the peritoneal cavity has not been involved. Among patients with peritoneal involvement, the mortality was highest among those under twelve years of age, but the general mortality was also high. However, cases were cited in which patients with profound wounds were saved by the use of prodigious amounts of blood and plasma, and the lesson to be learned is the necessity for large amounts of these lifesaving substances. Abdominal wounds in pregnant women have been almost universally fatal. On the other hand, few cases have been lost in maternity hospitals, even when such hospitals have been demolished, for it is usually possible to evacuate the patients in time. The prolapse of bowel in wounds of the abdomen apparently makes the prognosis much worse. Although one receives the impression that a large percentage of injuries to the bowel are fatal, statistics actually reveal a gross salvage of 40 to 50 per cent. The mortality in prolapse is about 80 per cent. Multiple wounds elsewhere in such patients are far greater in the present war, and the great lifesaving value of the resuscitation officers, with their plasma and blood, makes many seemingly moribund patients operable.

Abdominothoracic wounds contribute from 10 to 12 per cent of all wounds, as in the last conflict, with essentially the same recovery rate of 66 per cent. Injury to the right side offers a better prognosis, for only the liver is involved, contrasted with stomach, spleen and bowel on the left side. The respective mortalities are 50 and 70 per cent.

Blast injuries more frequently involve the thoracic than the abdominal viscera. This is also borne out by experimental work. Pathologically, multiple small subserous and submucous hemorrhages and tears are found. In naval warfare, this type of injury is sustained by survivors of sunken ships who are swimming in the water as depth charges explode.

EVANS MEMORIAL HOSPITAL

At a meeting at the Evans Memorial Hospital on November 21, Dr. Alvah H. Gordon, emeritus professor of medicine at McGill University, Montreal, spoke on "Bone Changes in Certain Medical Diseases." He emphasized the fact that bone has now become a recognized tissue with an active metabolism rather than merely a static structure with morphology. The discussion consisted of a lantern-slide demonstration of certain bone changes, common and rare, seen during a long experience.

Examples were shown of typical cases of certain metabolic diseases, such as gout, rickets, scurvy and lead poisoning. The fuzzy epiphyseal line in rickets was contrasted with the sharpness of that in scurvy, and the two were differentiated from congenital syphilis, which so often occurs in the same age group. Also briefly discussed were the changes of hyperparathyroidism.

The next group concerned hormonal imbalances. In the hyperpituitarism of Simmonds's disease, a characteristic widening of the sella turcica offers presumptive evidence of the diagnosis. A case of renal rickets, which was diagnosed at autopsy and was seen by many authorities during life, was considered a case of hypopituitarism. The relatively new concept that a postmenopausal osteoporosis is caused by lack of estrogens rather than by an inadequate diet has resulted from the work of Albright. Paget's disease, characterized by both an increase of growth and a degeneration of bone, is often found more or less accidentally or as the result of a pathologic fracture. The latter are usually transverse. Multiple myeloma can usually be found in several bones and clinically is on the borderline of malignancy. The unusual character of the bone metastases in carcinoma of the prostate and breast, which are oftener productive than destructive, was pointed out. Leukemia and leukemoid states frequently reveal bone changes, and these may also be osteosclerotic in aleukemic leukemia. There is an enlarged spleen, frequent backache and an elevation of the myelocyte count to high levels. An unusual case was cited in which such a process practically displaced all the active bone marrow; the spleen was enormously hypertrophied in an attempt to compensate for this displacement. Hand–Schüller–Christian's disease was mentioned in passing.

Finally, Dr. Gordon discussed achondroplasia, in which the short body is surpassed by even shorter arms. The mentality is rather good and is a definite point of differentiation of cretins and achondroplastics. Such people are invariably strong for their size. They should be classed as clever rather than intelligent, however.

BOOK REVIEWS

Arthritis and Allied Conditions. By Bernard I. Comroe, M.D. Second edition, thoroughly revised. 8°, cloth, 878 pp., with 242 illustrations. Philadelphia: Lea and Febiger, 1941. $9.00.

In the second edition of this book, a number of additions have been made to keep pace with the ever-expanding

knowledge of this group of diseases. A number of faults in the first edition have been corrected. The text is more carefully written, and the descriptions are clearer. There is logical arrangement of the material. The illustrations are excellent. Unfortunately, most of them have been borrowed from publications by other men. It would add to the value of the book if there were more sketches or photographs of necessary apparatus and braces, since many of these illustrations give no clear idea of the form of the apparatus or how it should be fitted. The book is complete, as full a presentation of knowledge as is possible. In the opinion of the reviewer, the weakest chapters are those dealing with related orthopedic lesions, in which the author's experience is necessarily limited; these could be omitted without lessening the value of the book. A well-selected bibliography follows each chapter.

Although this is an excellent discussion of arthritis, probably the best yet to appear in the English language, the average reader will be dismayed by its voluminousness. In an attempt to cover completely all diseases in which there is disability in the joints, the size of the book has become rather too large to attract a busy general practitioner. Those interested in treatment of chronic arthritis will find here an up-to-date summary of physiologic, pathologic and therapeutic data. Controversial subjects are presented without bias. But the author, mature in experience, has not hesitated to state his own opinion about them. This book should be welcomed by the physician who has the time and patience to read so large a volume, and it should be particularly helpful to those who treat chronic arthritis.

Stethoscopic Heart Records: Sounds, murmurs and arrhythmias. By George D. Geckeler, M.D. Columbia Records, Set M-600. Seven records. Price $12.75.

The faithful reproduction of heart sounds and murmurs by means of phonographic records is a feat that has tantalized and baffled sound engineers for nearly twenty years. The problems involved are extremely complex, and although this collection indicates that progress is being made, it also shows that there is still room for improvement. The technic of heart-sound reproduction involves the screening out of certain frequencies, to exaggerate other sounds that it is desired to bring out. The accomplishment of such selective exaggeration without undesirable distortion has seldom been achieved. In Dr. Geckeler's series, a good reproduction has been accomplished in about half the recordings. The most unsatisfactory are the attempts to reproduce gallop rhythm and faint mid-diastolic murmurs. The common arrhythmias, the aortic systolic and diastolic murmurs and the louder mitral diastolic murmurs are well illustrated. The best recordings are so very good that one can only hope that Dr. Geckeler will eventually succeed in bringing them all up to the same high standard. As they are, they should prove helpful in teaching auscultation to beginners.

Development Diagnosis: Normal and abnormal child development; clinical methods and practical applications. By Arnold Gesell, M.D., and Catherine S. Amatruda, M.D. 8°, cloth, 447 pp., with 20 illustrations. New York: Paul B. Hoeber, Incorporated, 1941. $6.50.

This is an elaborate experimental research on the development of behavior in infants from the time of birth up to the second year of life. The first part of the volume details what a child should be able to do, if it is both menially and physically normal, at the age of four, sixteen, twenty-eight and forty weeks and twelve, eighteen, twenty-four and thirty-six months. The methods of examination are given in great detail, with proper illustrations. This part of the book should be of value to all pediatricians in quickly estimating the capacity of a child.

The second part deals with various abnormal states: amentia, endocrine disorders, convulsive and other neurologic states, cerebral injury, prematurity, precocity and environmental retardation. This section of the work is not so elaborate as the first section, but is valuable in a general way. Other clinics, with larger experience, could use the material here presented as a basis for more extensive investigations. The most important chapter, on the clinical aspects of child adoption, is full of sound advice regarding this subject from the authors, who have had extensive experience.

A further section of the book deals with diagnosis, guidance and development supervision.

In general, this work is a fundamental text from a clinic of worldwide reputation. No other recommendation is needed.

Brucellosis (Undulant Fever), Clinical and Subclinical. By Harold J. Harris, M.D. Foreword by Walter M. Simpson, M.D. 8°, cloth, 286 pp., with 12 colored and 44 black-and-white illustrations. New York: Paul B. Hoeber, Incorporated, 1941. $5.50.

This monograph covers the history of brucellosis, as well as its etiology, epidemiology, pathology, symptomatology, diagnosis, prognosis, treatment and prophylaxis. Dr. Harris has had an active practice of medicine in a rural area and has based much of his work on the personal observations made on 250 patients with the disease. It is his opinion that infection with the disease is far greater than has generally been supposed, and that the chronic form constitutes 90 to 95 per cent of all brucellar infections. He states that this disease ranks with tuberculosis, syphilis and pneumonia in incidence, although not in mortality. He compares the disease to syphilis, because of its protean manifestations.

The major part of the book is devoted to symptomatology and diagnosis. There are colored illustrations of skin lesions and positive skin tests. Of particular interest to the practitioner is the composite picture of the most usual complaints encountered in the disease. Although farmers, dairymen and slaughterhouse workers contract the disease by direct contact, the greater part of the incidence is due to raw dairy products. The summer tourist may easily pick up the infection even though the greater part of his year is spent in areas where pasteurization is prevalent. Dr. Harris advocates the pasteurization of all milk and the destruction of all infected cattle, sheep, goats, pigs, horses and other domestic animals known to harbor the disease. Such a destruction would require a large expenditure of money, since it is estimated from surveys that between 11 and 20 per cent of all the cows in the United States are infected, and 20 per cent of the hogs in Iowa. Complete pasteurization seems possible, but at the present time, some communities and even entire states are so blind to the menace of raw milk that pasteurization is neglected.

This volume should be of great help to practitioners in communities where raw milk is consumed, and it would be a valuable addition to any physician's library.

(Notices on page xi)